APPROVED | O.G. FIG. —
BY | CLASS 435 | SUBCLASS 172.3
DRAFTSMAN

```
                                                                                                                    sau96I
                                                                                                                    haeIII
                                                                                                                    asuI
                                                                                                                   sau96I
                                                                                                                   nlaIV
                                                                                                                   hgiJII
                                                                                                                   eco0109I
                                                                                                                   bsp1286
                                                                                                                   banII
                                                                                                                   asuI
                                                                                                                  nlaIV
                                                                mnlI                                          aval apaI mnlI
                                                             mboII                                          mnlI  eco0109I     tth111I
  1      GGA CTT GTC TTC CTC GTC CTG CTG TTC CTC GGG GCC CTC GGA CTG
-18      Gly Leu Val Phe Leu Val Leu Leu Phe Leu Gly Ala Leu Gly Leu

                                                                haeIII
                                                               eaeI                                                 hinPI
                                                               cfrI                                                 hhaI
 46 TGT CTG GCT GGC CGT AGG AGA AGG AGT GTT CAG TGG TGC GCC GTA TCC
 -3 Cys Leu Ala Gly Arg Arg Arg Ser Val Gln Trp Cys Ala Val Ser

                                                                haeIII
                                                               mnlI
                                                             aval haeI
 94 CAA CCC GAG GCC ACA AAA TGC TTC CAA TGG CAA AGG AAT ATG AGA AAA
 14 Gln Pro Glu Ala Thr Lys Cys Phe Gln Trp Gln Arg Asn Met Arg Lys

                                                                   mnlI          fnu4HI
                                                               sau96I            bbvI                 pleI
                                                               haeIII           aluI                  hinfI          bsrI
                                                               asuI           pvuII                 bsmaI         fokI
142 GTG CTG GGC CCT CCT GTC AGC TGC ATA AAG AGA GAC TCC CCC ATC CAG
 30 Val Arg Gly Pro Pro Val Ser Cys Ile Lys Arg Asp Ser Pro Ile Gln

                                                                haeIII
                                                               haeI
                                                           scrFI                          haeIII
                                                           ecoRII                        sau96I
                                                           bstNI                         asuI   sfaNI
190 TGT ATC CAG GCC ATT GCG GAA AAC AGG GCC GAT GCT GTG ACC CTT GAT
 46 Cys Ile Gln Ala Ile Ala Glu Asn Arg Ala Asp Ala Val Thr Leu Asp

                                                                                               sau96I
                                                                                               nlaIV
                                                                                          scrFI
                                                                                          ecoRII
                                                                                          bstNI
                                                                                        haeIII
                                                                                      stuI    haeIII
                                                                              mnlI  haeI    asuI
238 GGT GGT TTC ATA TAC GAG GCA GGC CTG GCC CCC TAC AAA CTG CGA CCT
 62 Gly Gly Phe Ile Tyr Glu Ala Gly Leu Ala Pro Tyr Lys Leu Arg Pro
```

FIG.—1A

APPROVED BY DRAFTSMAN
O.G. FIG. CLASS SUBCLASS

```
                                    sau96I
                                    avaII
                                    asuI
          fnu4HI       accI     nlaIV
286 GTA GCG GCG GAA GTC TAC GGG ACC GAA AGA CAG CCA CGA ACT CAC TAT
 78 Val Ala Ala Glu Val Tyr Gly Thr Glu Arg Gln Pro Arg Thr His Tyr

                                                fnu4HI
                                mboII           bbvI          aluI
                          hphI                fnu4HI aluI     pvuII
334 TAT GCC GTG GCT GTG GTG AAG AAG GGC GGC AGC TTT CAG CTG AAC GAA
 94 Tyr Ala Val Ala Val Val Lys Lys Gly Gly Ser Phe Gln Leu Asn Glu

                                              haeIII       sau96I
                                            stuI           avaII
                                  bglI      haeI           asuI       fokI
382 CTG CAA GGT CTG AAG TCC TGC CAC ACA GGC CTT CGC AGG ACC GCT GGA
110 Leu Gln Gly Leu Lys Ser Cys His Thr Gly Leu Arg Arg Thr Ala Gly

                                                                   sau961
                                                                   avaII
                                                                   asuI
                                                                 nlaIV
430 TGG AAT GTC CCT ACA GGG ACA CTT CGT CCA TTC TTG AAT TGG ACG GGT
126 Trp Asn Val Pro Thr Gly Thr Leu Arg Pro Phe Leu Asn Trp Thr Gly

            hgiJII           aluI
            bsp1286        fnu4HI
            banII          bbvI                    ddeI      aluI
          ddeI           mnlI pvuII           mboII        pvuII
478 CCA CCT GAG CCC ATT GAG GCA GCT GTG CAG TTC TTC TCA GCC AGC TGT
142 Pro Pro Glu Pro Ile Glu Ala Ala Val Gln Phe Phe Ser Ala Ser Cys

          mspI
          hpaII
        scrFI
        nciI
        cauII
526 GTT CCC GGT GCA GAT AAA GGA CAG TTC CCC AAC CTG TGT CGC CTG TGT
158 Val Pro Gln Ala Asp Lys Gly Gln Phe Pro Asn Leu Cys Arg Leu Cys

                                                      nlaIV
                                                    scrFI
                                                    ecoRII
                                                 mnlI bstNI      rsaI
574 GCG GGG ACA GGG GAA AAC AAA TGT GCC TTC TCC TCC CAG GAA CCG TAC
174 Ala Gly Thr Gly Glu Asn Lys Cys Ala Phe Ser Ser Gln Glu Pro Tyr
```

FIG.-1B

APPROVED BY DRAFTSMAN
O.G. FIG. CLASS SUBCLASS

```
                      nlaIV
                      hgiCI
          aluI        banI                  ddeI  bsmaI          bsmaI
622 TTC AGC TAC TCT GGT GCC TTC AAG TGT CTG AGA GAC GGG GCT GGA GAC
190 Phe Ser Tyr Ser Gly Ala Phe Lys Cys Leu Arg Asp Gly Ala Gly Asp

                                                 sau96I
                                                 avaII
                                                 asuI
                                                ppuMI
                              hgiAI              eco0109I
                              bsp1286          mnlI                mnlI
670 GTG GCT TTT ATC AGA GAG AGC ACA GTG TTT GAG GAC CTG TCA GAC GAG
206 Val Ala Phe Ile Arg Glu Ser Thr Val Phe Glu Asp Leu Ser Asp Glu

718 GCT GAA AGG GAC GAG TAT GAG TTA CTC TGC CCA GAC AAC ACT CGG AAG
222 Ala Glu Arg Asp Glu Tyr Glu Leu Leu Cys Pro Asp Asn Thr Arg Lys

                                                  scrFI
                                                  nciI
                                                  mspI
                                                  hpaII
                                                  cauII
                                                 xmaI sau96I
                                                 smaI nlaIV
                                                 scrFI
                                                 nciI avaII
                                                 cauII
                                                 avaI asuI
                                              sau96I ppuMI
                                              haeIII nlaIV
    bsrI                                      asuI   eco0109I       nlaIII
766 CCA GTG GAC AAG TTC AAA GAC TGC CAT CTG GCC CGG GTC CCT TCT CAT
238 Pro Val Asp Lys Phe Lys Asp Cys His Leu Ala Arg Val Pro Ser His

                                                    sfaNI
                                                   fokI                mboII
    bglI          draIII                        mnlI                hinfI
814 GCC GTT GTG GCA CGA AGT GTG AAT GGC AAG GAG GAT GCC ATC TGG AAT
254 Ala Val Val Ala Arg Ser Val Asn Gly Lys Glu Asp Ala Ile Trp Asn

              scrFI
              ecoRII
              bstNI                                          hphI
862 CTT CTC CGC CAG GCA CAG GAA AAG TTT GGA AAG GAC AAG TCA CCG AAA
270 Leu Leu Arg Gln Ala Gln Glu Lys Phe Gly Lys Asp Lys Ser Pro Lys
```

FIG.-1C

APPROVED BY DRAFTSMAN
O.G. FIG. CLASS SUBCLASS

```
                                                          sau3AI
                                                          mboI
                                                          dpnI
                                                       xhoII
          aluI                                         bstYI
       bstXI          nlaIV                          bglII
910 TTC CAG CTC TTT GGC TCC CCT AGT GGG CAG AAA GAT CTG CTG TTC AAG
286 Phe Gln Leu Phe Gly Ser Pro Ser Gly Gln Lys Asp Leu Leu Phe Lys

                                        nlaIV
                                        hgiCI
    pleI                             mnlI  bsp1286   mnlI
    hinfI                          taqI  banI    avaI          hinfI
958 GAC TCT GCC ATT GGG TTT TCG AGG GTG CCC CCG AGG ATA GAT TCT GGG
302 Asp Ser Ala Ile Gly Phe Ser Arg Val Pro Pro Arg Ile Asp Ser Gly

                    mspI
          styI      hpaII
      rsaI      nlaIV                        fokI            mnlI
1006 CTG TAC CTT GGC TCC GGC TAC TTC ACT GCC ATC CAG AAC TTG AGG AAA
318 Leu Tyr Leu Gly Ser Gly Tyr Phe Thr Ala Ile Gln Asn Leu Arg Lys

                                  mspI
                                  hpaII      thaI
                                 scrFI       fnuDII
                                 ncII        bstUI
           mnlI          fnu4HI            hinPI
       mnlI              bbvI cauII        hhaI
1054 AGT GAG GAG GAA GTG GCT GCC CGG CGT GCG CGG GTC GTG TGG TGT GCG
344 Ser Glu Glu Glu Val Ala Ala Arg Arg Ala Arg Val Val Trp Cys Ala

                            hinPI
                           mstI
                           fspI
                         fnu4HI
                        aluI hhaI            bstXI
                   alwNI bbvI                bsrI
1102 GTG GGC GAG CAG GAG CTG CGC AAG TGT AAC CAG TGG AGT GGC TTG AGC
350 Val Gly Glu Gln Glu Leu Arg Lys Cys Asn Gln Trp Ser Gly Leu Ser

         fnu4HI                          mnlI
         bbvI       bspMI    mnlI haeIII          mnlI     sfaNI
1150 GAA GGC AGC GTG ACC TGC TCC TCG GCC TCC ACC ACA GAG GAC TGC ATC
366 Glu Gly Ser Val Thr Cys Ser Ser Ala Ser Thr Thr Glu Asp Cys Ile

      scrFI
      ecoRII                                bstXI
      bstNI                        aluI  sfaNI nlaIII      fokI   mnlI
1198 GCC CTG GTG CTG AAA GGA GAA GCT GAT GCC ATG AGT TTG GAT GGA GGA
382 Ala Leu Val Leu Lys Gly Glu Ala Asp Ala Met Ser Leu Asp Gly Gly
```

FIG.-1D

APPROVED BY DRAFTSMAN
O.G. FIG. CLASS SUBCLASS

```
                        nlaIII                  nlaIV       scrFI
                       sphI                     hgiCI       ecoRII
              rsaI     nspCIx                   banI        bstNI
1246 TAT GTG TAC ACT GCA TGC AAA TGT GGT TTG GTG CCT GTC CTG GCA GAG
 398 Tyr Val Tyr Thr Ala Cys Lys Cys Gly Leu Val Pro Val Leu Ala Glu

                                                sau3AI
                                                mboI
                                                dpnI
                                                alwI
1294 AAC TAC AAA TCC CAA CAA AGC AGT GAC CCT GAT CCT AAC TGT GTG GAT
 414 Asn Tyr Lys Ser Gln Gln Ser Ser Asp Pro Asp Pro Asn Cys Val Asp

                                                          sau3AI
                                                          mboI
          ecoNI          ecoRV                            dpnI
1342 AGA CCT GTG GAA GGA TAT CTT GCT GTG GCG GTG GTT AGG AGA TCA GAC
 430 Arg Pro Val Glu Gly Tyr Leu Ala Val Ala Val Val Arg Arg Ser Asp

                    scrFI
                    ecoRII
                    bstNI
1390 ACT AGC CTT ACC TGG AAC TCT GTG AAA GGC AAG AAG TCC TGC CAC ACC
 446 Thr Ser Leu Thr Trp Asn Ser Val Lys Gly Lys Lys Ser Cys His Thr

                                                    haeIII
                                                nlaIII
                                               styI sau96I      mboII
                          pstI                 ncoI asuI       earI
1438 GCC GTG GAC AGG ACT GCA GGC TGG AAT ATC CCC ATG GGC CTG CTC TTC
 462 Ala Val Asp Arg Thr Ala Gly TrP Asn Ile Pro Met Gly Leu Leu Phe

                  nlaIV
                 hgiJII
                 bsp1286
                 banII                          sspI                 aluI bsp1286
1486 AAC CAG ACG GGC TCC TGC AAA TTT GAT GAA TAT TTC AGT CAA AGC TGT
 478 Asn Gln Thr Gly Ser Cys Lys Phe Asp Glu Tyr Phe Ser Gln Ser Cys

                              sau3AI
                              mboI
                              DpnI
          scrFI               xhoII
          ecoRII              bstYI            hgiAI
          bstNI        aval   bglII            bsp1286
1534 GCC CCT GGG TCT GAC CCG AGA TCT AAT CTC TGT GCT CTG TGT ATT GGC
 484 Ala Pro Gly Ser Asp Pro Arg Ser Asn Leu Cys Ala Leu Cys Ile Gly
```

FIG.-1E

APPROVED BY DRAFTSMAN
O.G. FIG. CLASS SUBCLASS

```
                    hphI                    bsp1286
1582 GAC GAG CAG GGT GAG AAT AAG TGC GTG CCC AAC AGC AAT GAG AGA TAC
 510 Asp Glu Gln Gly Glu Asn Lys Cys Val Pro Asn Ser Asn Glu Arg Tyr

                                      nlaIV
                                      hgiCI
                                      banI scrFI
                                  mspI    ecoRII
                    bsrI          hpaII   bstNI  ddeI bsmI       bsmaI
1630 TAC GGC TAC ACT GGG GCT TTC CGG TGC CTG GCT GAG AAT GCT GGA GAC
 526 Tyr Gly Tyr Thr Gly Ala Phe Arg Cys Leu Ala Glu Asn Ala Gly Asp

1678 GTT GCA TTT GTG AAA GAT GTC ACT GTC TTG CAG AAC ACT GAT GGA AAT
 542 Val Ala Phe Val Lys Asp Val Thr Val Leu Gln Asn Thr Asp Gly Asn

                                                                fnu4HI
                                                                bbvI
                                                             hinPI
              mnlI nlaIII  ddeI             aluI               hhaI
1726 AAC AAT GAG GCA TGG GCT AAG GAT TTG AAG CTG GCA GAC TTT GCG CTG
 558 Asn Asn Glu Ala Trp Ala Lys Asp Leu Lys Leu Ala Asp Phe Ala Leu

             taqI                                                fnu4HI
          mnlI                                      mnlI          bbvI
        bglI                                      ddeI           aluI
1774 CTG TGC CTC GAT GGC AAA CGG AAG CCT GTG ACT GAG GCT AGA AGC TGC
 574 Leu Cys Leu Asp Gly Lys Arg Lys Pro Val Thr Glu Ala Arg Ser Cys

                 sau96I
                 nlaIV
              nlaIII
             styI haeIII
             ncoI asuI    hinfI nlaIII        bsmaI  fokI
1822 CAT CTT GCC ATG GCC CCG AAT CAT GCC GTG GTG TCT CGG ATG GAT AAG
 590 His Leu Ala Met Ala Pro Asn His Ala Val Val Ser Arg Met Asp Lys

                                fnu4HI
              ecoNI      alwNI bbvI
1870 GTG GAA CGC CTG AAA CAG GTG CTG CTC CAC CAA CAG GCT AAA TTT GGG
 606 Val Glu Arg Leu Lys Gln Val Leu Leu His Gln Gln Ala Lys Phe Gly

             sau3AI
             mboI           mspI
             dpnI           hpaII
            xhoII         scrFI
            bstYI         nciI
            alwI          cauII                          bsrI
1919 AGA AAT GGA TCT GAC TGC CCG GAC AAG TTT TGC TTA TTC CAG TCT GAA
 622 Arg Asn Gly Ser Asp Cys Pro Asp Lys Phe Cys Leu Phe Gln Ser Glu
```

FIG.—1F

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

```
                                                                    haeIII
                                                                    haeI
                                                                    eaeI          styI
                                                        ddeI        cfrI    pleI ncoI
                                                      draIII        balI    hinfI
1966 ACC AAA AAC CTT CTG TTC AAT GAC AAC ACT GAG TGT CTG GCC AGA CTC
 638 Thr Lys Asn Leu Leu Phe Asn Asp Asn Thr Glu Cys Leu Ala Arg Leu

                                                    sau96I
                                                    avaII
                                                    asuI
     nlaIII          ndeI        sspI     nlaIV
2014 CAT GGC AAA ACA ACA TAT GAA AAA TAT TTG GGA CCA CAG TAT GTC GCA
 654 His Gly Lys Thr Thr Tyr Glu Lys Tyr Leu Gly Pro Gln Tyr Val Ala

                                                                scrFI
                                                                ecoRII
                                  hgiAI                         bstNI
                                  bsp1286    mnlI      mnlI
2062 GGC ATT ACT AAT CGT AAA AAG TGC TCA ACC TCC CCC CTC CTG GAA GCC
 670 Gly Ile Thr Asn Leu Lys Lys Cys Ser Thr Ser Pro Leu Leu Glu Ala

                ddeI
              mstII
              mnlI                                  sau96I
              eco81I                          mboII haeIII
        ecoRI bsu36I                        mboII  asuI aluI
2110 TGT GAA TTC CTC AGG AAG TAA  AACCGAAGAA GATGGCCCAG CTCCCCAAGA
 685 Cys Glu Phe Leu Arg Lys □C*

                                                                   styI
                                                                 haeIII
                                                                sau96I
                                        mboII    scrFI          asuI
          ddeI                         earI      ecoRII       nlaIV
         mnlI                        aluI        bstNI        eco□109I nlaIV
2161 AAGCCTCAGC CATTCACTGC CCCCAGCTCT TCTCCCCAGG TGTGTTGGGG CCTTGGCTCC

     ecoNI                    fokI                                  ddeI
2221 CCTGCTGAAG GTGGGGATTG CCCATCCATC TGCTTACAAT TCCCTGCTGT CGTCTTAGCA

2281 AGAAGTAAAA TGAGAAATTT TGTTGATATT CAAAAAAAA

>LENGTH: 2319
```

FIG.-1G

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

```
  1 GACTCCTAGG GGCTTGCAGA CCTAGTGGGA GAGAAAGAAC ATCGCAGCAG CCAGGCAGAA CCAGGACAGG TGAGGTGCAG GCTGGCTTTC CTCTCGCAGC
101 GCGGTGTGGA GTCCTGTCCT GCCTCAGGGC TTTTCGGAGC CTGGATCCTC AAGGAACAAG TAGACCTGGC CGCGGGGAGT GGGGAGGGAA GGGGTGTCTA
201 TTGGGCAACA GGGCGGCAAA GCCCTGAATA AAGGGGCGCA GGGCAGGCGC AAGTGCAGAG CCTTCGTTTG CCAAGTCGCC TCCAGACCGC AGAC ATG AAA CTT
-19                                                                                                        M   K   L
304 GTC TTC CTC GTC CTG CTG TTC CTC GGG GCC CTC GGA CTG TGT CTG GCT GGC CGT AGG AGA AGG AGT GTT CAG TGG TGC GCC GTA TCC
-16 V   F   L   V   L   L   F   L   G   A   L   G   L   C   L   A   G   R   R   R   R   S   V   Q   W   C   A   V   S
391 CAA CCC GAG GCC ACA AAA TGC TTC CAA TGG CAA AGG AAT ATG AGA AAA GTG CGT GGC CCT CCT GTC AGC TGC ATA AAG AGA GAC TCC
 14 Q   P   E   A   T   K   C   F   Q   W   Q   R   N   M   R   K   V   R   G   P   P   V   S   C   I   K   R   D   S
478 CCC ATC CAG TGT ATC CAG GCC ATT GCG GAA AAC AGG GCC GAT GCT GTG ACC CTT GAT GGT GGT TTC ATA TAC GAG GCA GGC CTG GCC
 43 P   I   Q   C   I   Q   A   I   A   E   N   R   A   D   A   V   T   L   D   G   G   F   I   Y   E   A   G   L   A
565 CCC TAC AAA CTG CGA CCT GTA GCG GCG GAA GTC TAC GGG ACC GAA AGA CAG CCA CGA ACT CAC TAT TAT GCC GTG GCT GTG GTG AAG
 72 P   Y   K   L   R   P   V   A   A   E   V   Y   G   T   E   R   Q   P   R   T   H   Y   Y   A   V   A   V   V   K
652 AAG GGC GGC AGC TTT CAG CTG AAC GAA CTG CAA GGT CTG AAG TCC TGC CAC ACA GGC CTT CGC AGG ACC GCT GGA TGG AAT GTC CCT
101 K   G   G   S   F   Q   L   N   E   L   Q   G   L   K   S   C   H   T   G   L   R   R   T   A   G   W   N   V   P
739 ACA GGG ACA CTT CGT CCA TTC TTG AAT TGG ACG GGT CCA CCT GAG CCC ATT GAG GCA GCT GTG GCC AGG TTC TTC TCA GCC AGC TGT
130 T   G   T   L   R   P   F   L   N   W   T   G   P   P   E   P   I   E   A   A   V   A   R   F   F   S   A   S   C
826 GTT CCC GGT GCA GAT AAA GGA CAG TTC CCC AAC CTG TGT CGC CTG TGT GCG GGG ACA GGG GAA AAC AAA TGT GCC TTC TCC TCC CAG
159 V   P   G   A   D   K   G   Q   F   P   N   L   C   R   L   C   A   G   T   G   E   N   K   C   A   F   S   S   Q
913 GAA CCG TAC TTC AGC TAC TCT GGT GCC TTC AAG TGT CTG AGA GAC GGG GCT GGA GAC GTG GCT TTT ATC AGA GAG AGC ACA GTG TTT
188 E   P   Y   F   S   Y   S   G   A   F   K   C   L   R   D   G   A   G   D   V   A   F   I   R   E   S   T   V   F
1000 GAG GAC CTG TCA GAC GAG GCT GAA AGG GAC GAG TAT GAG TTA CTC TGC CCA GAC AAC ACT CGG AAG CCA GTG GAC AAG TTC AAA GAC
217 E   D   L   S   D   E   A   E   R   D   E   Y   E   L   L   C   P   D   N   T   R   K   P   V   D   K   F   K   D
1087 TGC CAT CTG GCC CGG GTC CCT TCT CAT GCC GTT GTG GCA CGA AGT GTG AAT GGC AAG GAG GAT GCC ATC TGG AAT CTT CTC CGC CAG
246 C   H   L   A   R   V   P   S   H   A   V   V   A   R   S   V   N   G   K   E   D   A   I   W   N   L   L   R   Q
1174 GCA CAG GAA AAG TTT GGA AAG GAC AAG TCA CCG AAA TTC CAG CTC TTT GGC TCC CCT AGT GGG CAG AAA GAT CTG CTG TTC AAG GAC
275 A   Q   E   K   F   G   K   D   K   S   P   K   F   Q   L   F   G   S   P   S   G   Q   K   D   L   L   F   K   D
1261 TCT GCC ATT GGG TTT TCG AGG GTG CCC CCG AGG ATA GAT TCT GGG CTG TAC CTT GGC TCC GGC TAC TTC ACT GCC ATC CAG AAC TTG
304 S   A   I   G   F   S   R   V   P   P   R   I   D   S   G   L   Y   L   G   S   G   Y   F   T   A   I   Q   N   L
1348 AGG AAA AGT GAG GAG GAA GTG GCT GCC CGG CGT GCG CGG GTC GTG TGG TGT GCG GTG GGC GAG CAG GAG CTG CGC AAG TGT AAC CAG
333 R   K   S   E   E   E   V   A   A   R   R   A   R   V   V   W   C   A   V   G   E   Q   E   L   R   K   C   N   Q
```

FIG.-2A

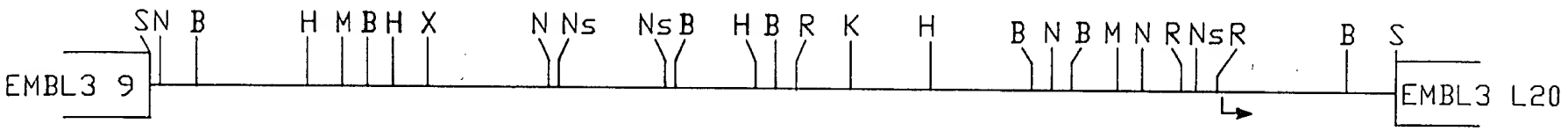
APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

```
1435 TGG AGT GGC TTG AGC GAA GGC AGC GTG ACC TGC TCC TCG GCC TCC ACC ACA GAG GAC TGC ATC GCC CTG GTG CTG AAA GGA GAA GCT
 362 W   S   G   L   S   E   G   S   V   T   C   S   S   A   S   T   T   E   D   C   I   A   L   V   L   K   G   E   A
1522 GAT GCC ATG AGT TTG GAT GGA GGA TAT GTG TAC ACT GCA TGC AAA TGT GGT TTG GTG CCT GTC CTG GCA GAG AAC TAC AAA TCC CAA
 391 D   A   M   S   L   D   G   G   Y   V   Y   T   A   C   K   C   G   L   V   P   V   L   A   E   N   Y   K   S   Q
1609 CAA AGC AGT GAC CCT GAT CCT AAC TGT GTG GAT AGA CCT GTG GAA GGA TAT CTT GCT GTG GCG GTG GTT AGG AGA TCA GAC ACT AGC
 420 Q   S   S   D   P   D   P   N   C   V   D   R   P   V   E   G   Y   L   A   V   A   V   V   R   R   S   D   T   S
1696 CTT ACC TGG AAC TCT GTG AAA GGC AAG AAG TCC TGC CAC ACC GCC GTG GAC AGG ACT GCA GGC TGG AAT ATC CCC ATG GGC CTG CTC
 449 L   T   W   N   S   V   K   G   K   K   S   C   N   T   A   V   D   R   T   A   G   W   N   I   P   M   Q   L   L
1783 TTC AAC CAG ACG GGC TCC TGC AAA TTT GAT GAA TAT TTC AGT CAA AGC TGT GCC CCT GGG TCT GAC CCG AGA TCT AAT CTC TGT GCT
 478 F   N   Q   T   G   S   C   K   F   D   E   Y   F   S   Q   S   C   A   P   G   S   D   P   R   S   N   L   C   A
1870 CTG TGT ATT GGC GAC GAG CAG GGT GAG AAT AAG TGC GTG CCC AAC AGC AAC GAG AGA TAC TAC GGC TAC ACT GGG GCT TTC CGG TGC
 507 L   C   I   G   D   E   Q   G   E   N   K   C   V   P   N   S   N   E   R   Y   Y   G   Y   T   G   A   F   R   C
1957 CTG GCT GAG AAT GCT GGA GAC GTT GCA TTT GTG AAA GAT GTC ACT GTC TTG CAG AAC ACT GAT GGA AAT AAC AAT GAG GCA TGG GCT
 536 L   A   E   N   A   G   D   V   A   F   V   K   D   V   T   V   L   Q   N   T   D   G   N   N   N   E   A   W   A
2044 AAG GAT TTG AAC CTG GCA GAC TTT GCG CTG CTG TGC CTC GAT GGC AAA CGG AAG CCT GTG ACT GAC GCT AGA AGC TGC CAT CTT GCC
 565 K   D   L   K   L   A   D   F   A   L   L   C   L   D   G   K   R   K   P   V   T   E   A   R   S   C   H   L   A
2131 ATG GCC CCG AAT CAT GCC GTG GTG TCT CGG ATG GAT AAG GTG GAA CGC CTG AAA CAG GTG CTG CTC CAC CAA CAG GCT AAA TTT GGG
 594 M   A   P   N   H   A   V   V   S   R   M   D   K   V   E   R   L   K   Q   V   L   L   H   Q   Q   A   K   F   G
2218 AGA AAT GGA TCT GAC TGC CCG GAC AAG TTT TGC TTA TTC CAG TCT GAA ACC AAA AAC CTT CTG TTC AAT GAC AAC ACT GAG TGT CTG
 623 R   N   G   S   D   C   P   D   K   F   C   L   F   Q   S   E   T   K   N   L   L   F   N   D   N   T   E   C   L
2305 GCC AGA CTC CAT GGC AAA ACA ACA TAT GAA AAA TAT TTG GGA CCA CAG TAT GTC GCA GGC ATT ACT AAT CTG AAA AAG TGC TCA ACC
 652 A   R   L   H   G   K   T   T   Y   E   K   Y   L   G   P   Q   Y   V   A   G   I   T   N   L   K   K   C   S   T
2392 TCC CCC CTC CTG GAA GCC TGT GAA TTC CTC AGG AAG TAA  AACCGAAGAA GATGGCCCAG CTCCCCAAGA AAGCCTCAGC CATTCACTGC CCCCAGCTCT
 681 S   P   L   L   E   A   C   E   F   L   R   K   D
2491 TCTCCCCAGG TGTGTTGGGG CCTTGGCTCC CCTGCTGAAG GTGGGGATTG CCCATCCATC TGCTTACAAT TCCCTGCTGT CGTCTTAGCA AGAAGTAAAA
2591 TGAGAAATTT TGTTGATATT CAAAAAAAA
```

FIG.-2B

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

RESTRICTION MAP OF 5' - FLANKING REGION OF αS1 CASEIN GENE



S - SalI

B - BalII

R - EcoRI

H - HindIII

M - SmaI

N - NcoI

Ns - NsiI

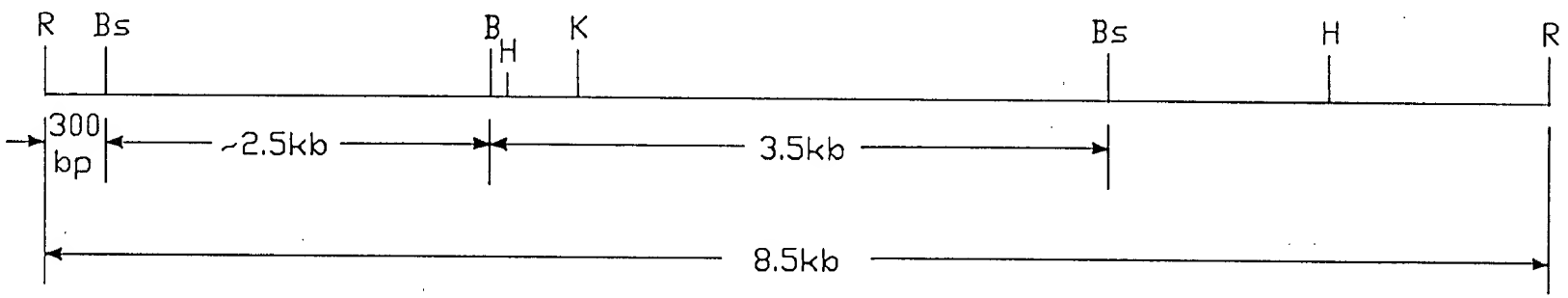
X - XhoI

K - KpnI

FIG.-3

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

RESTRICTION MAP OF 3' FLANKING
REGION OF α S1 CASEIN GENE



1kb

R - EcoRI

Bs - Bst EII

B - BamHI

H - HindIII

K - KpnI

FIG.-4

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

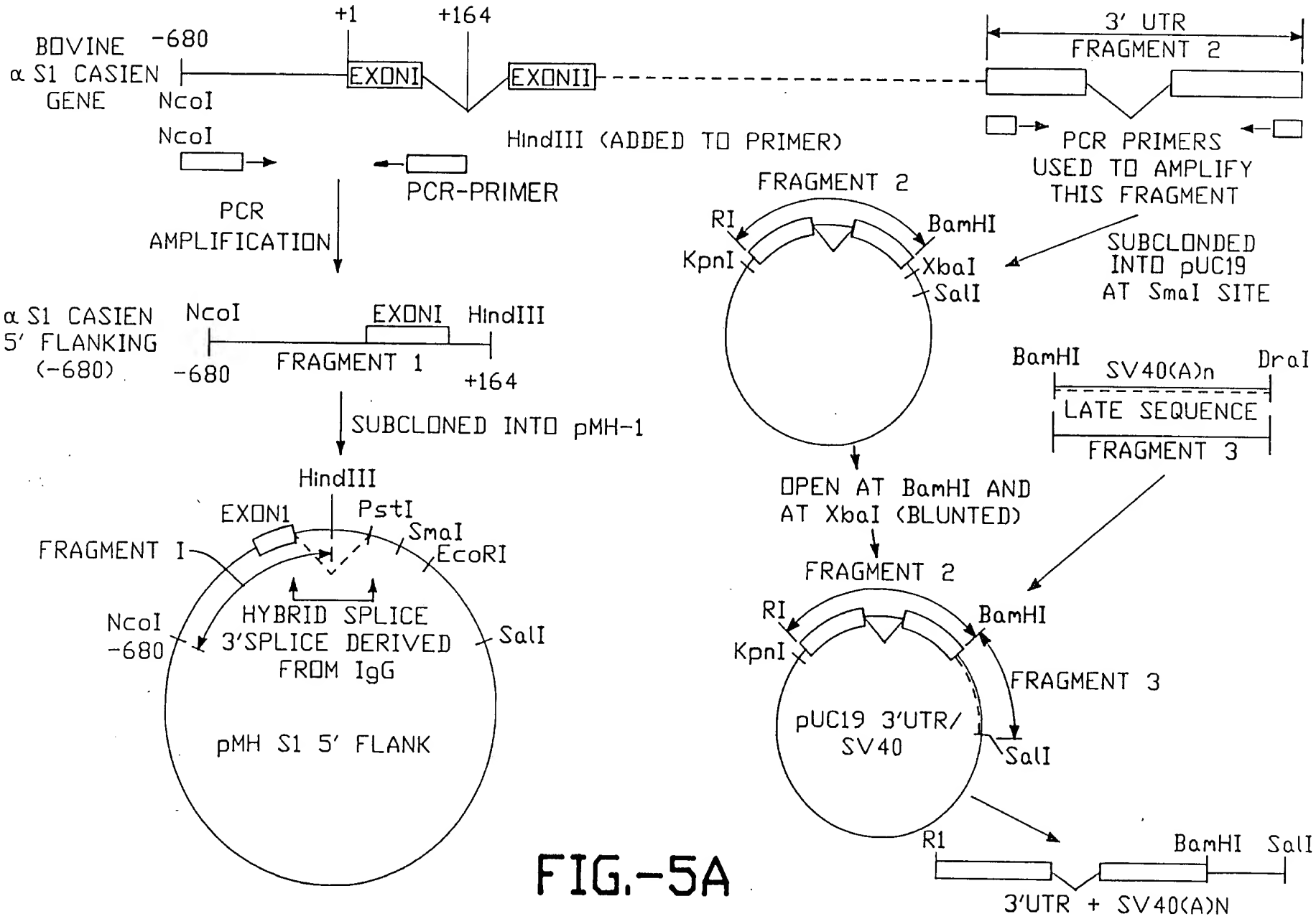


FIG.-5A

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

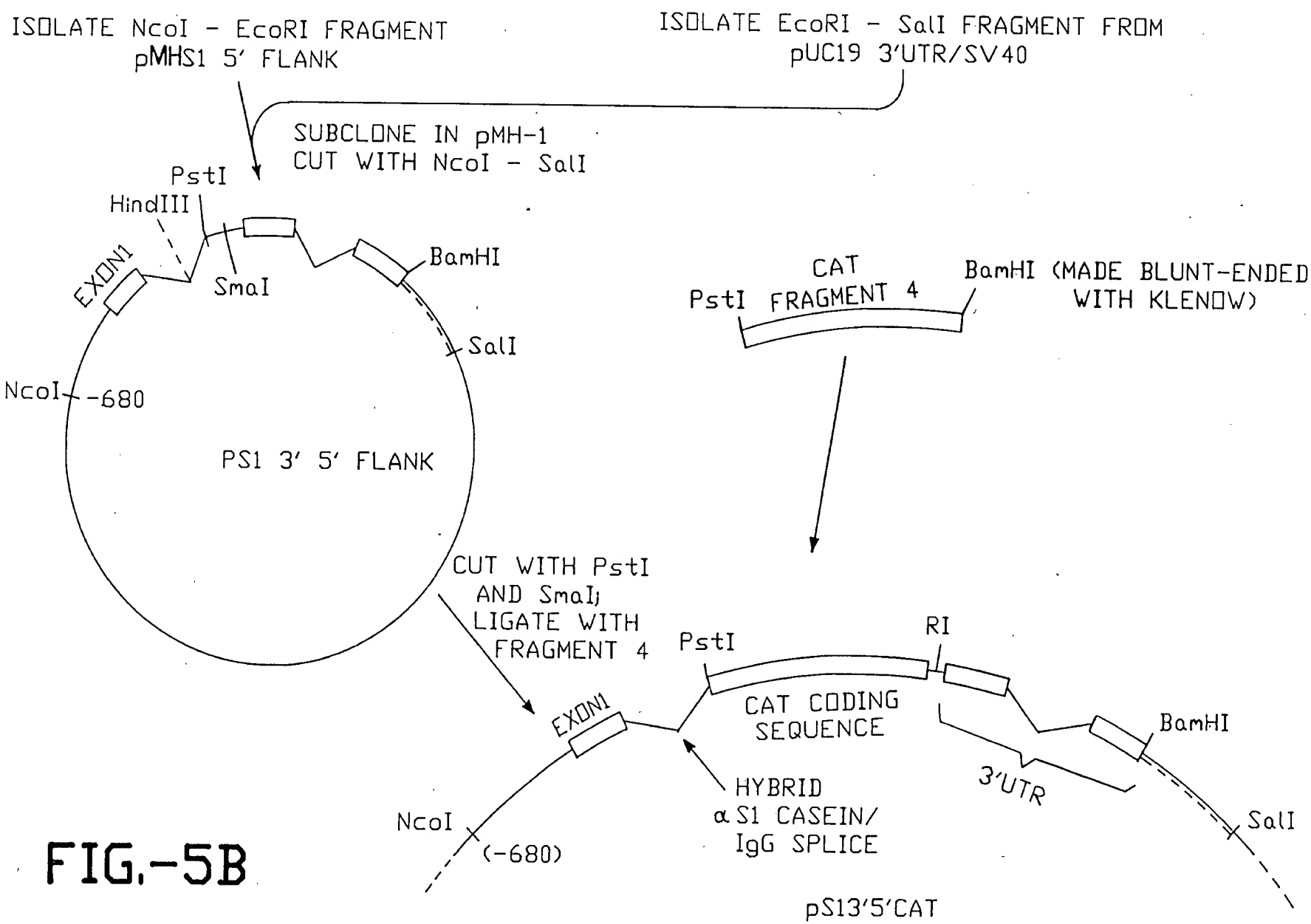


FIG.-5B

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

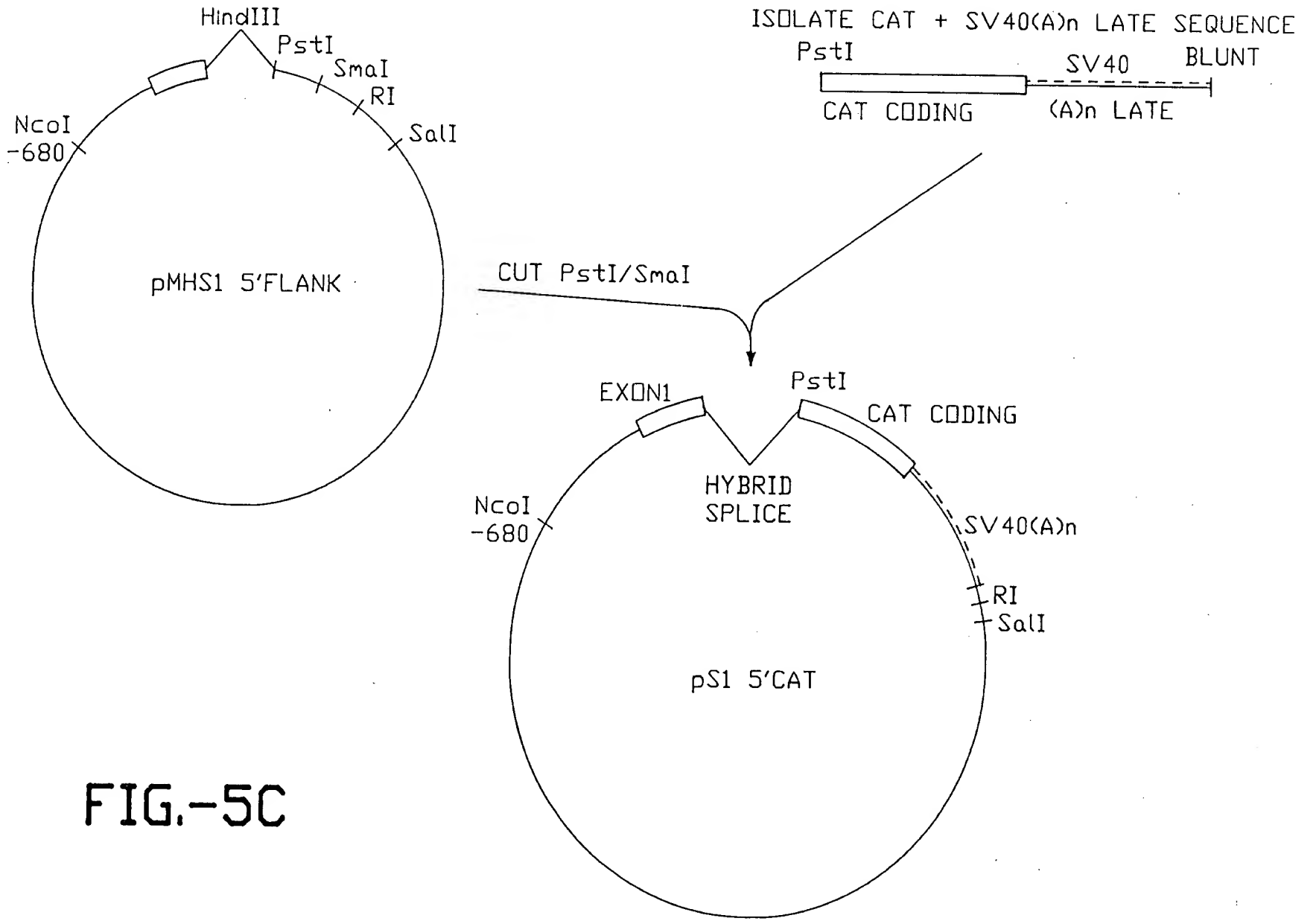


FIG.-5C

APPROVED | O.G. FIG. | SUBCLASS
BY | CLASS
DRAFTSMAN

NAME pMH-1

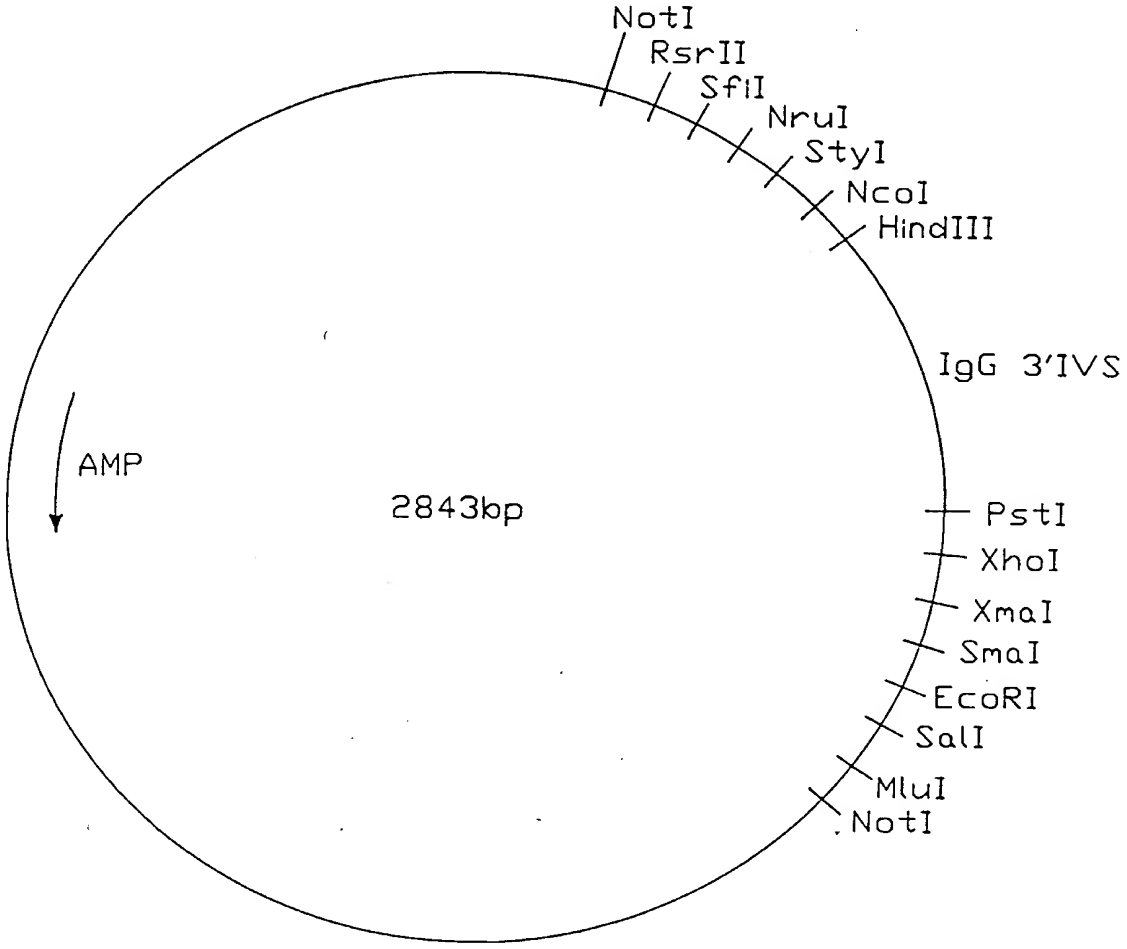
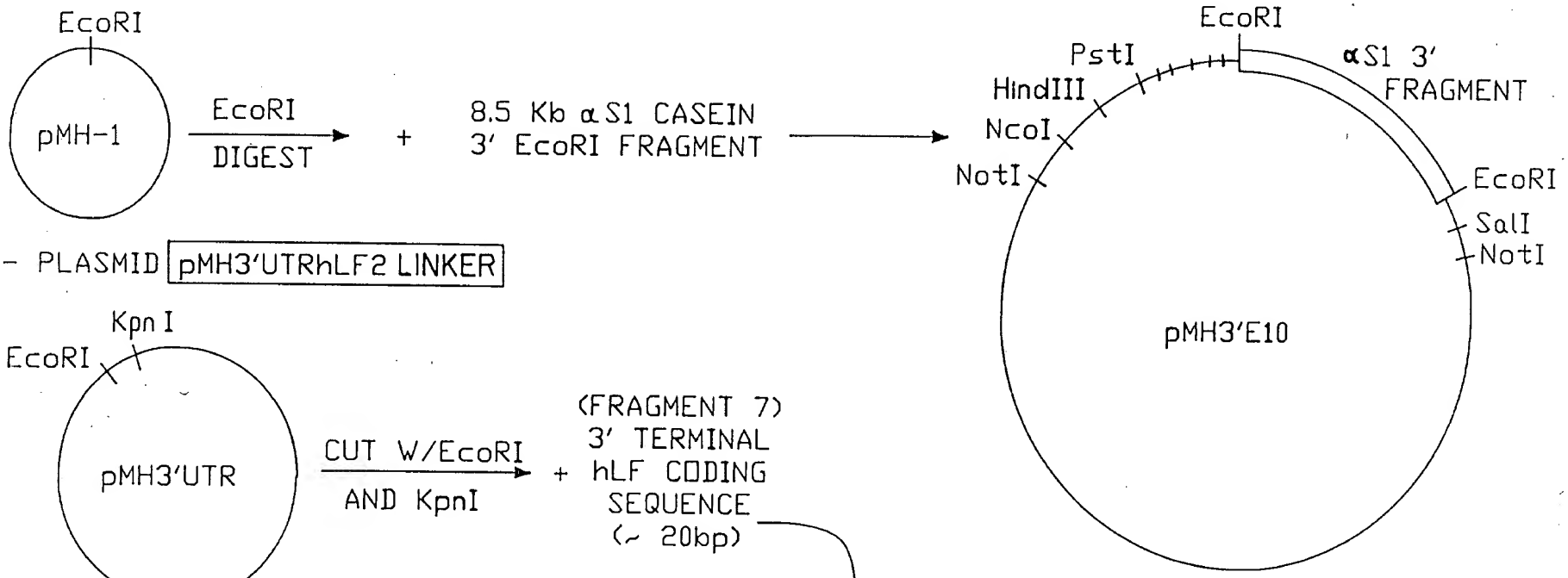


FIG.-6

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

- PLASMID pMH3'E10 CONTAINS ~ 8.5Kb EcoRI FRAGMENT OF THE 3'-END OF αS1 CASEIN. pMH-1 WAS CUT W/EcoRI + LIGATED TO THIS FRAGMENT



- PLASMID pMH3'UTRhLF2 LINKER

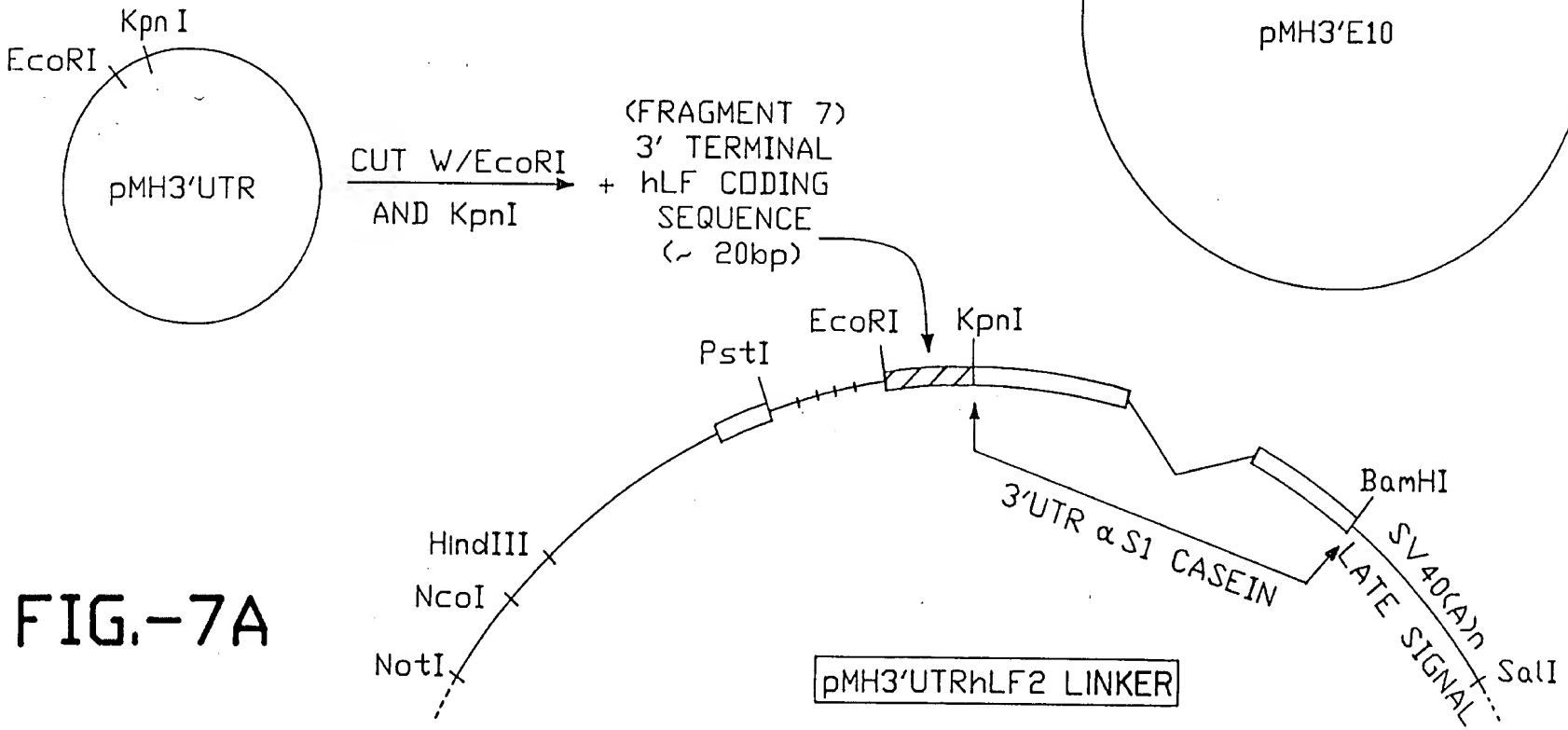
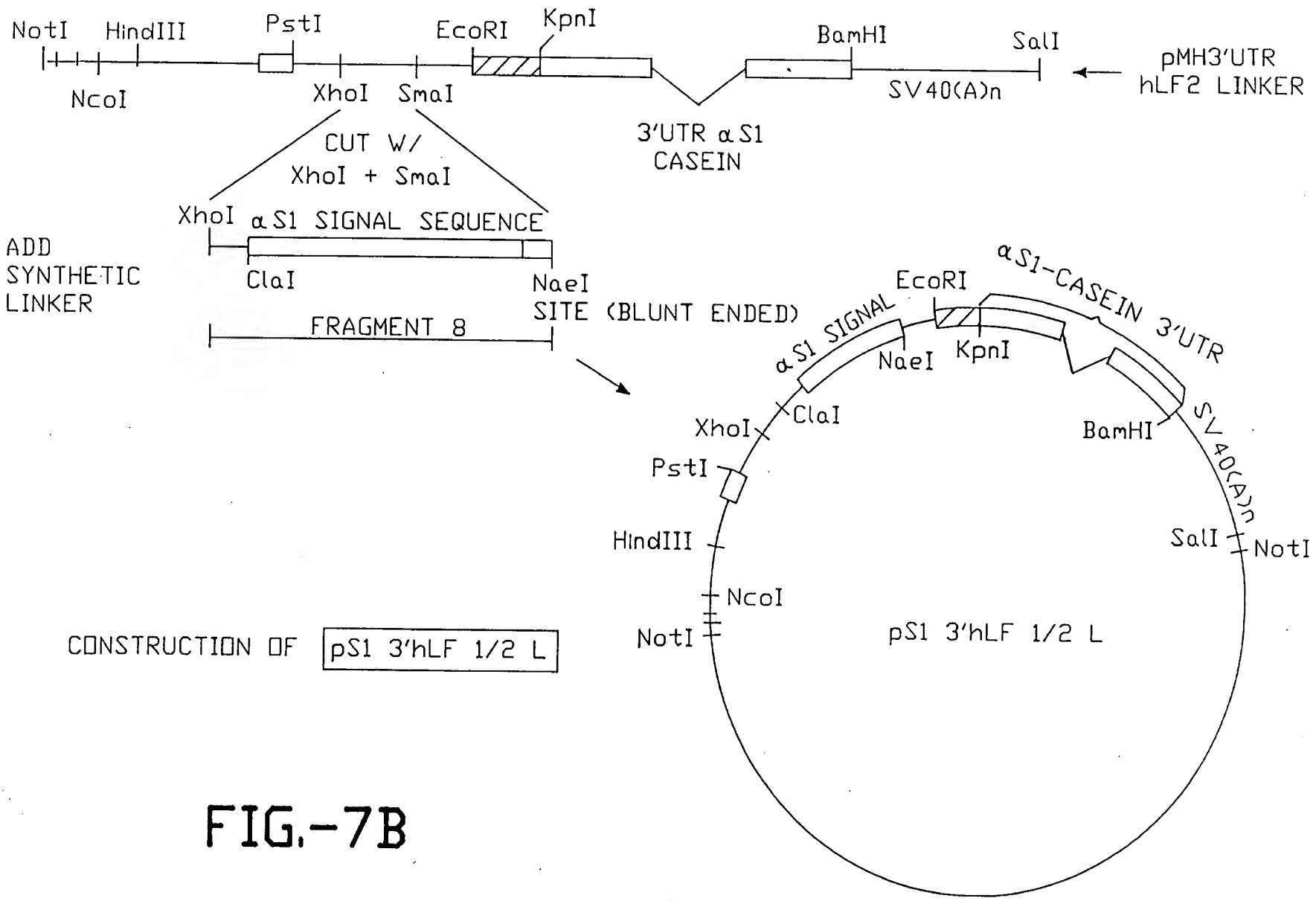


FIG.-7A

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS



CONSTRUCTION OF pS1 3'hLF 1/2 L

FIG.-7B

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

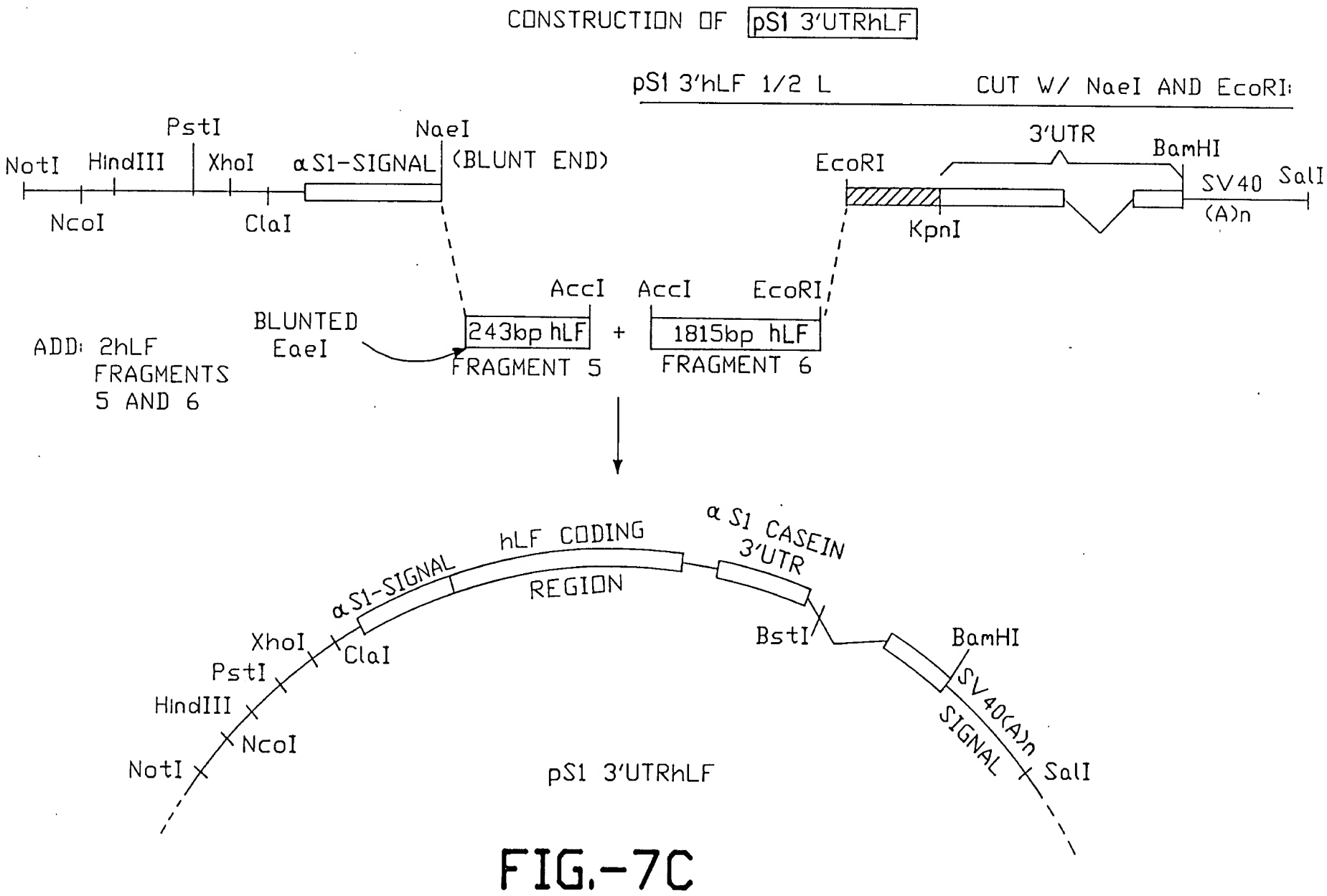


FIG.-7C

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS

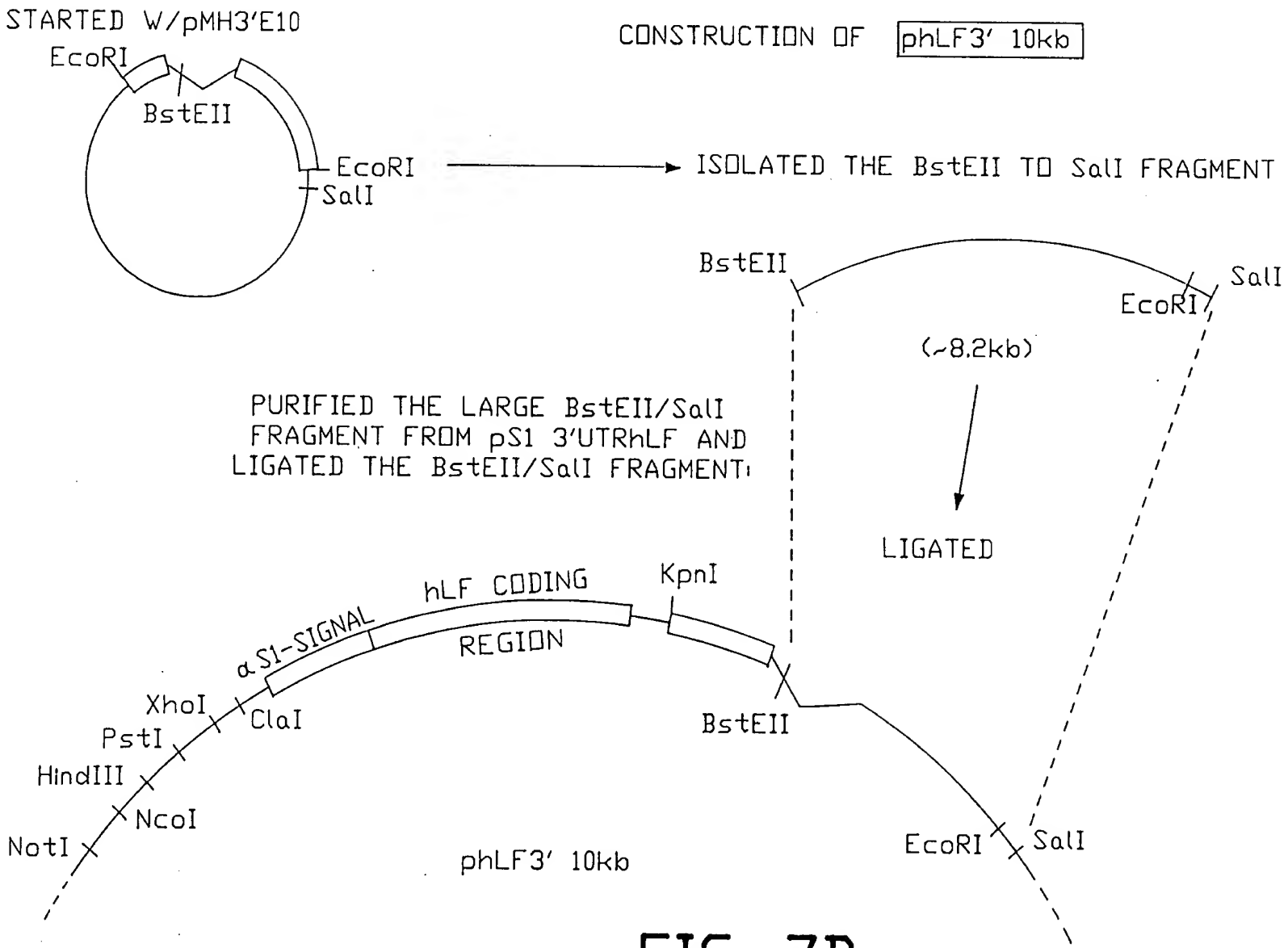
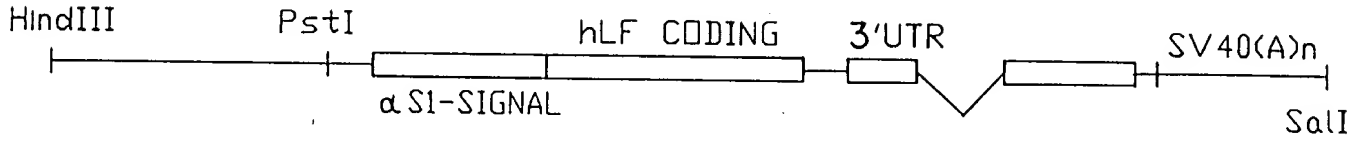


FIG.-7D

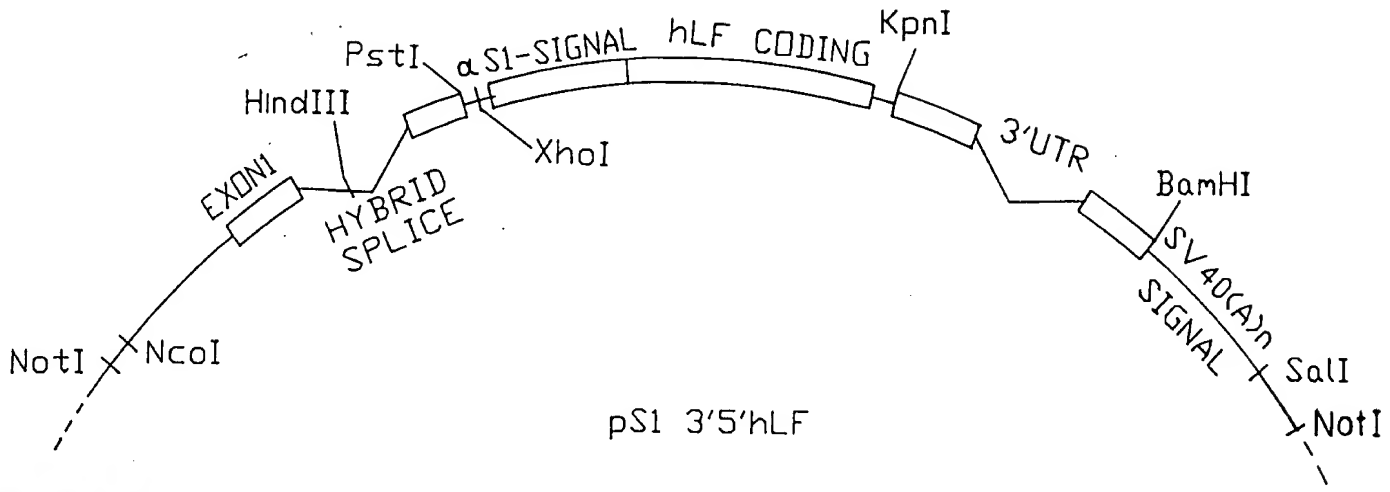
APPROVED BY DRAFTSMAN	O.G. FIG.	
	CLASS	SUBCLASS

CONSTRUTION OF pS1 3'5'hLF

STARTED W/pS1 3'UTRhLF. CUT W/HindIII AND SalI AND PURIFIED THIS FRAGMENT CONTAINING THE αS1-CASEIN SIGNAL SEQUENCE, hLF CODING REGION, αS1UTR AND SV40(A)n.



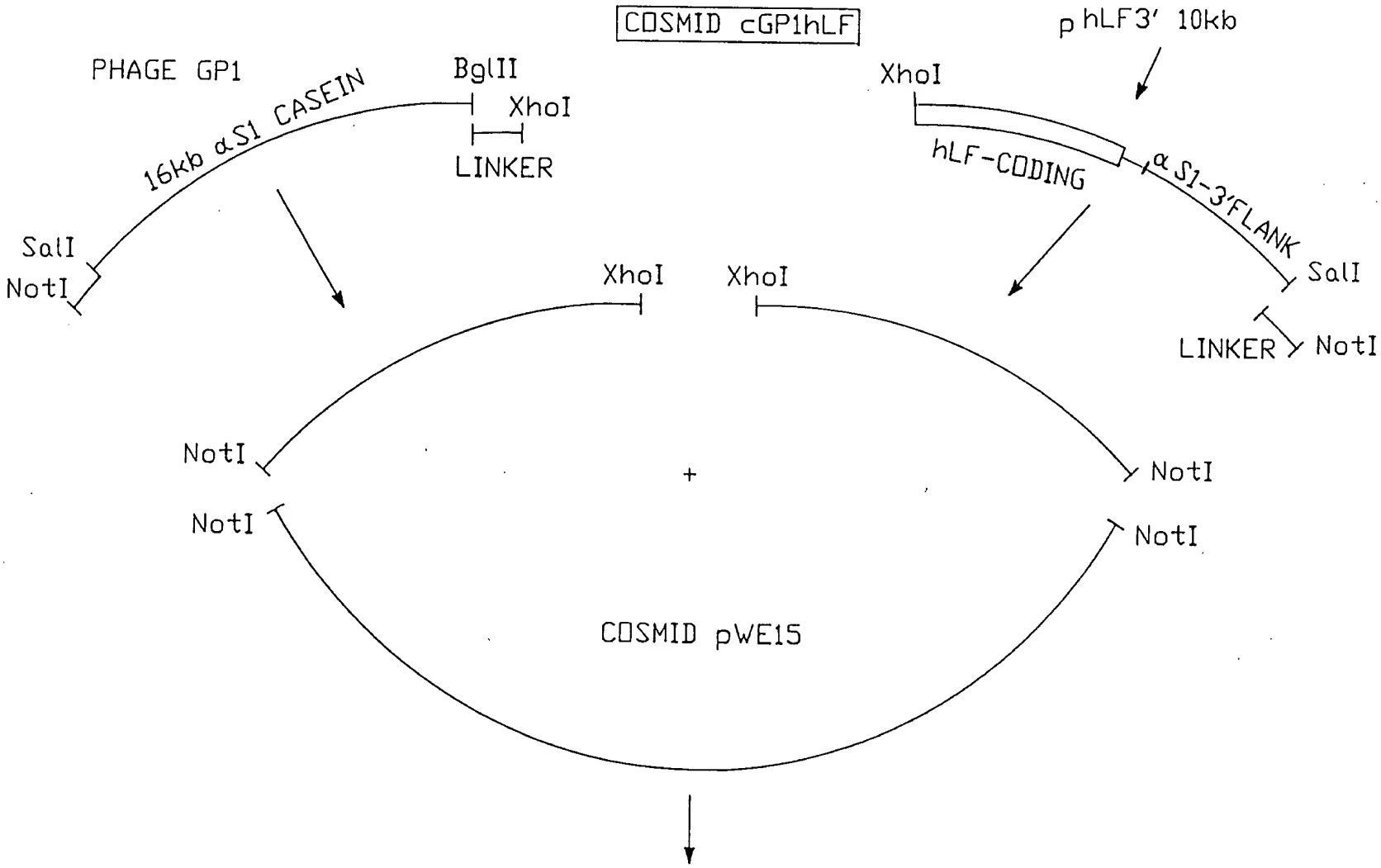
SUBCLONED INTO HindIII/SalI
CUT pMHS1 5' FLANK TO YIELD:



NOTE: pS1 5'hLF WAS MADE BY CUTTING pS13'5'hLF W/KpnI AND BamHI, FOLLOWED BY BLUNTING THE ENDS AND RELIGATING. THIS ELIMINATES THE SPLICED 3'UTR REGION.

FIG.-7E

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS



3 WAY LIGATION. THE DNA FROM THIS COSMID IS PREPARED BY CUTTING WITH NotI AND PURIFYING THE EXPRESSION SEQUENCE PRIOR TO MICROINJECTION.

FIG.-7F

APPROVED BY DRAFTSMAN
O.G. FIG. CLASS SUBCLASS

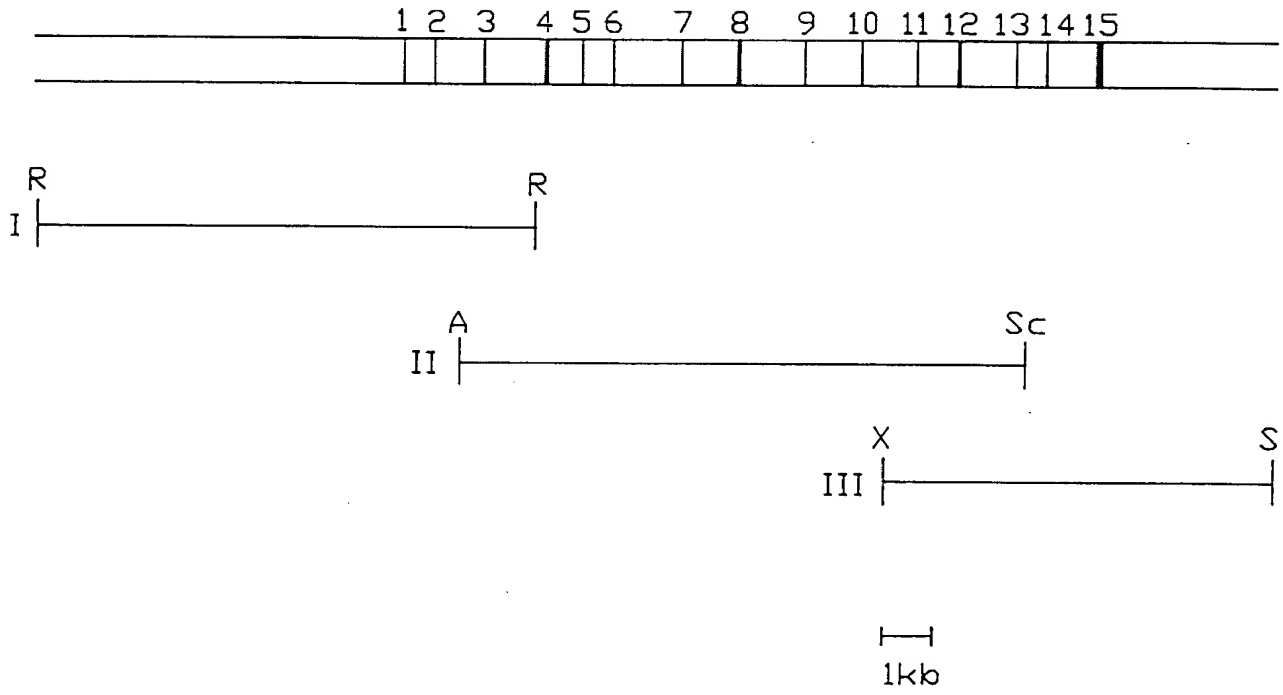


FIG.-8A

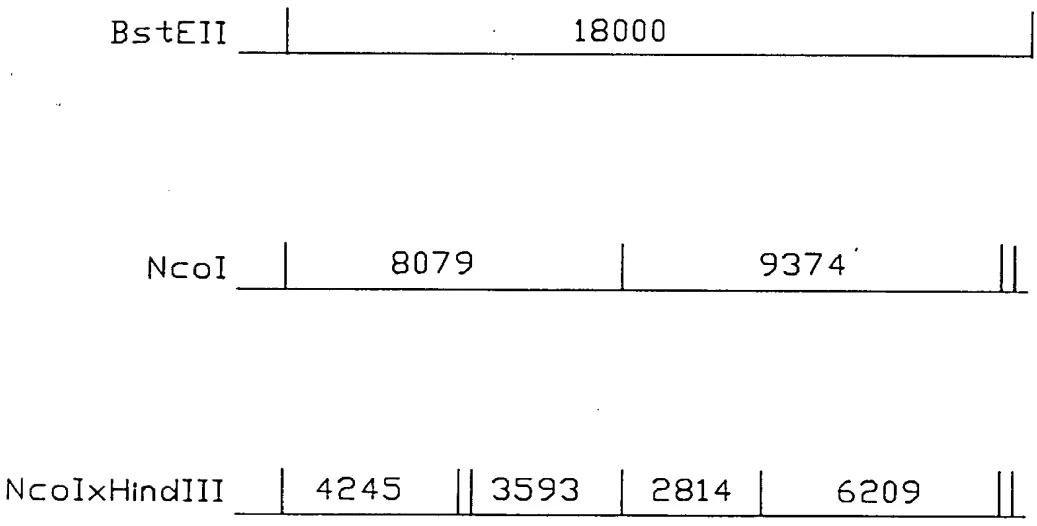
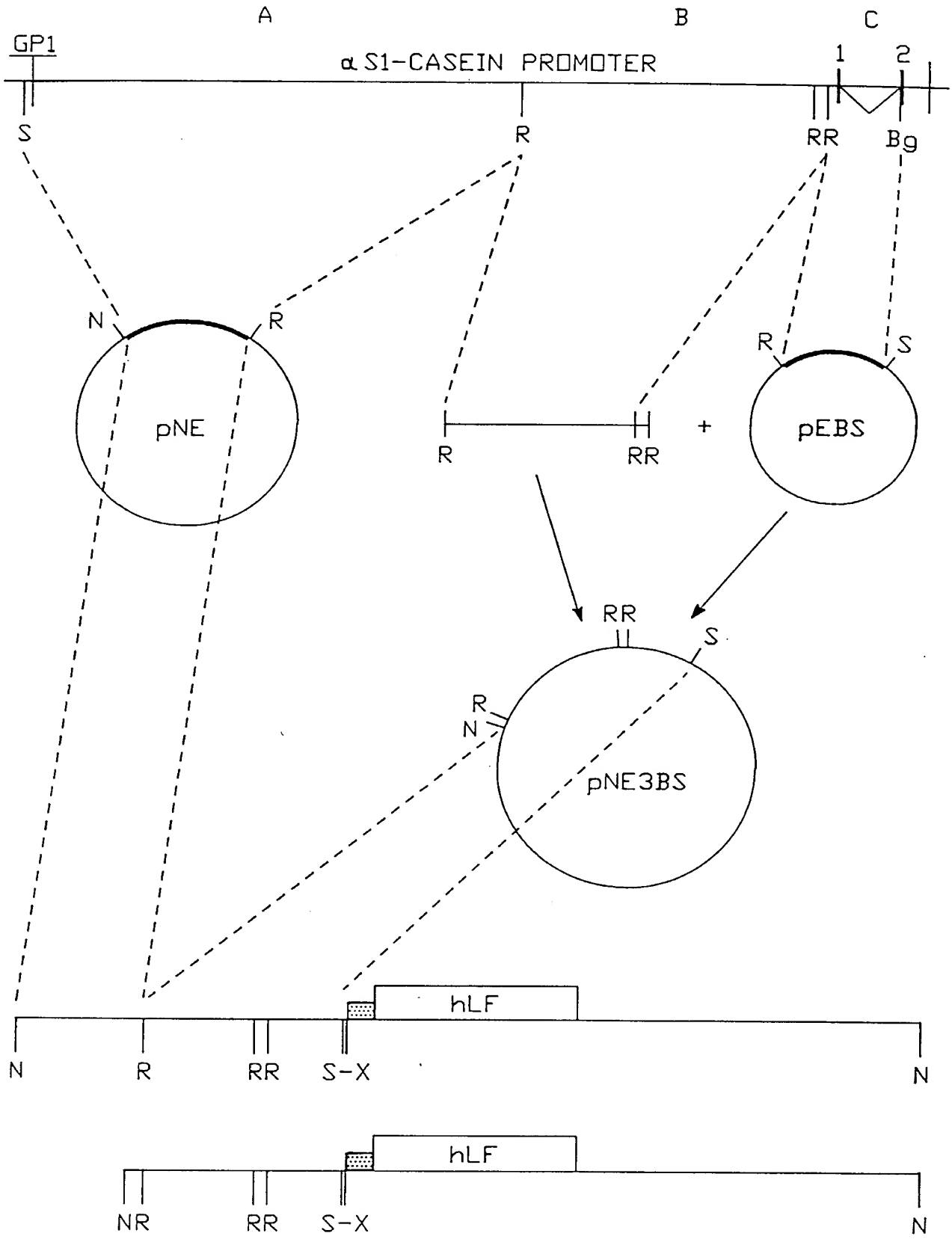


FIG.-8B

APPROVED BY DRAFTSMAN
O.G. FIG.
CLASS
SUBCLASS



S=SalI R=EcoRI Bg=BglII N=NotI X=XhoI

FIG.-9

O.G. FIG.
SUBCLASS
CLASS
APPROVED BY DRAFTSMAN

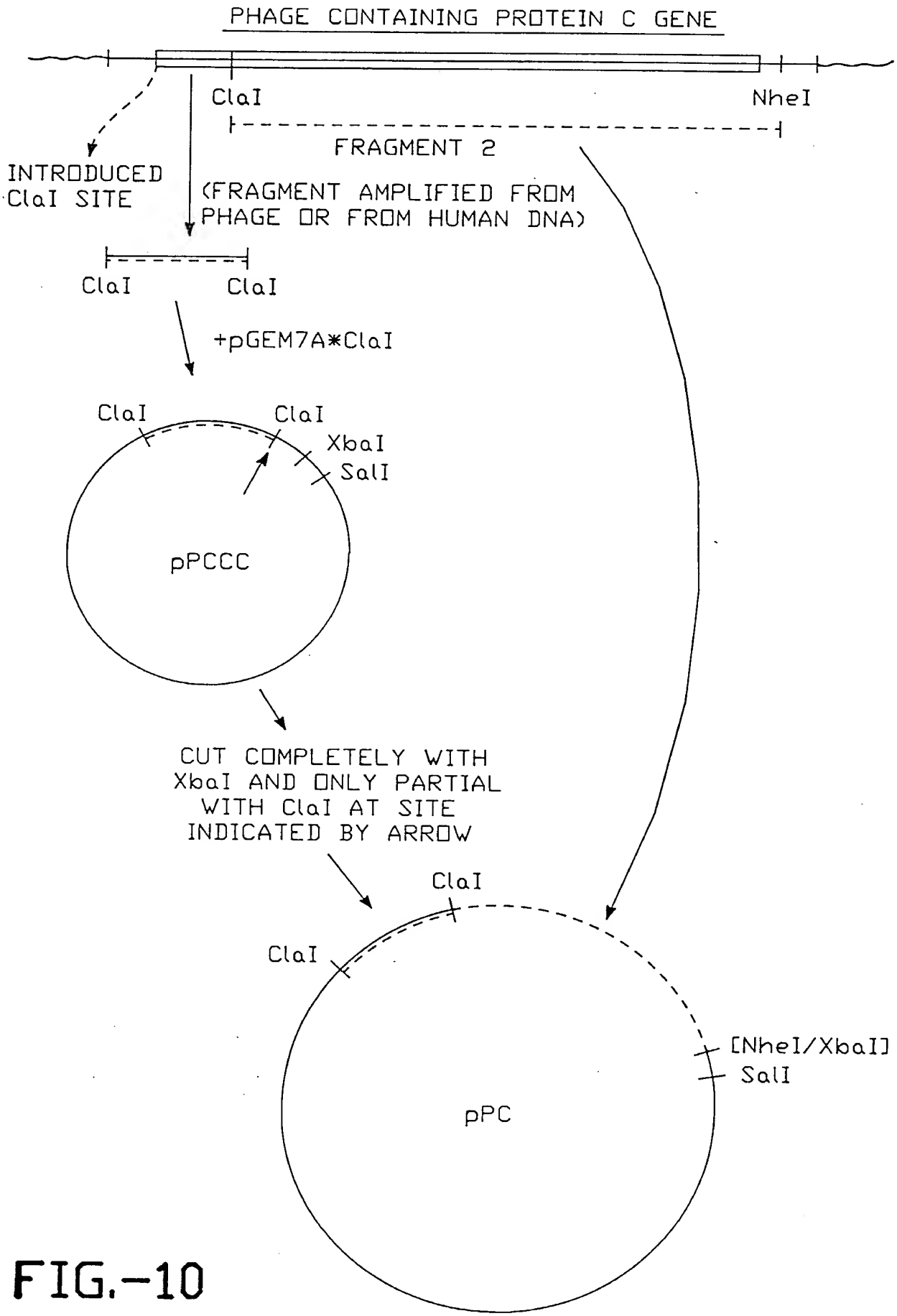


FIG.-10

APPROVED BY DRAFTSMAN | O.G. FIG. CLASS | SUBCLASS

5′- ATCACCTTGA TCATCAACCC AGCTTGCTGC TTCTTCCCAG

TCTTGGGTTC AAG gtattatgta tacatataac aaaatttcta tgattttcct ctgtctcatc

tttcattctt cactaatacg cagttgtaac ttttctatgt gattgcaagt attggtactt tcctatgata

tactgttagc aagcttgagg tgtggcaggc ttgagatctg gccatacact tgagtgacaa tgacatccac

tttgcctttc tctccacag GTGTCCACTC CCAGGTCCAA CTGCAG -3′

FIG.-11

O.G. FIG. | CLASS | SUBCLASS | APPROVED BY DRAFTSMAN

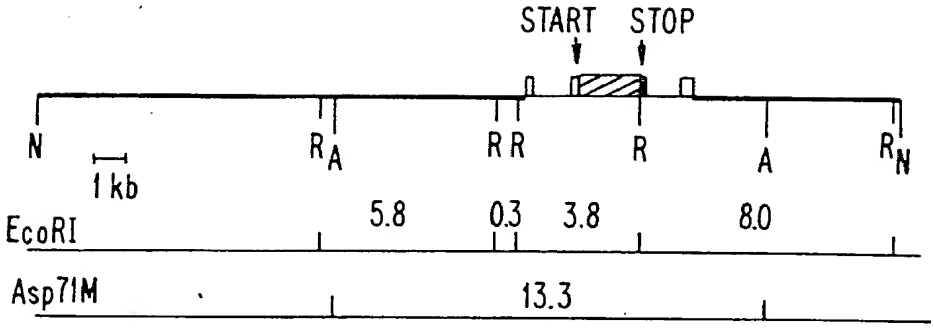


FIG. 12A.

COSMIDS CONTAINING ENTIRE hLF GENE (NOT DRAWN TO SCALE)

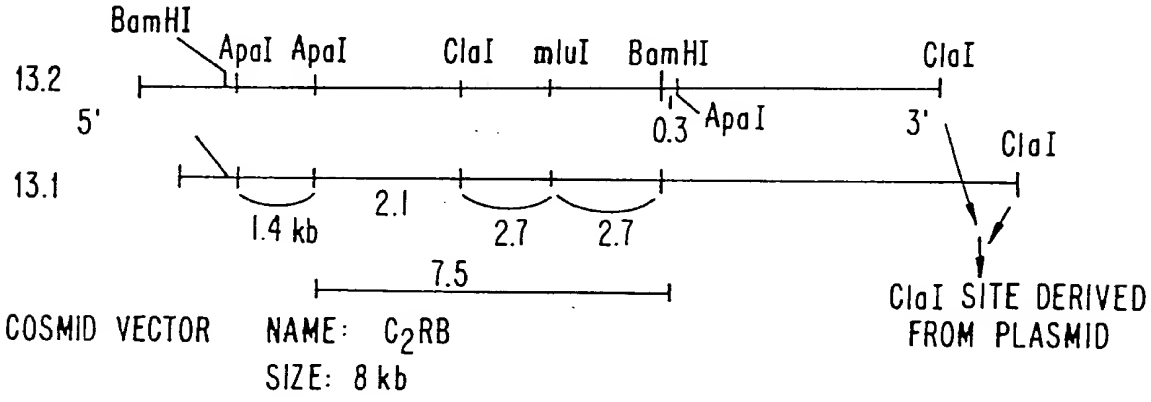


FIG. 13.

9 kb Bam HI hLF FRAGMENT IN pUC19

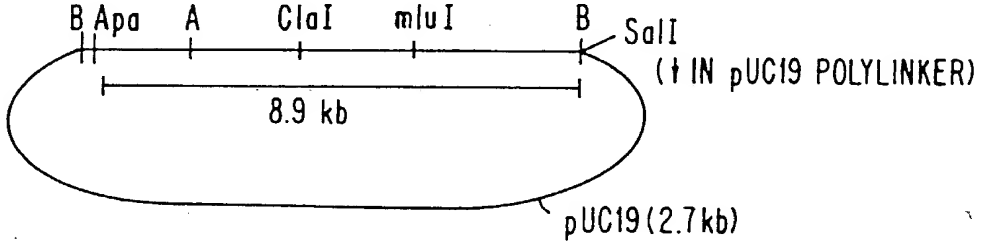


FIG. 14.

APPROVED BY DRAFTSMAN
O.G. FIG.
CLASS
SUBCLASS

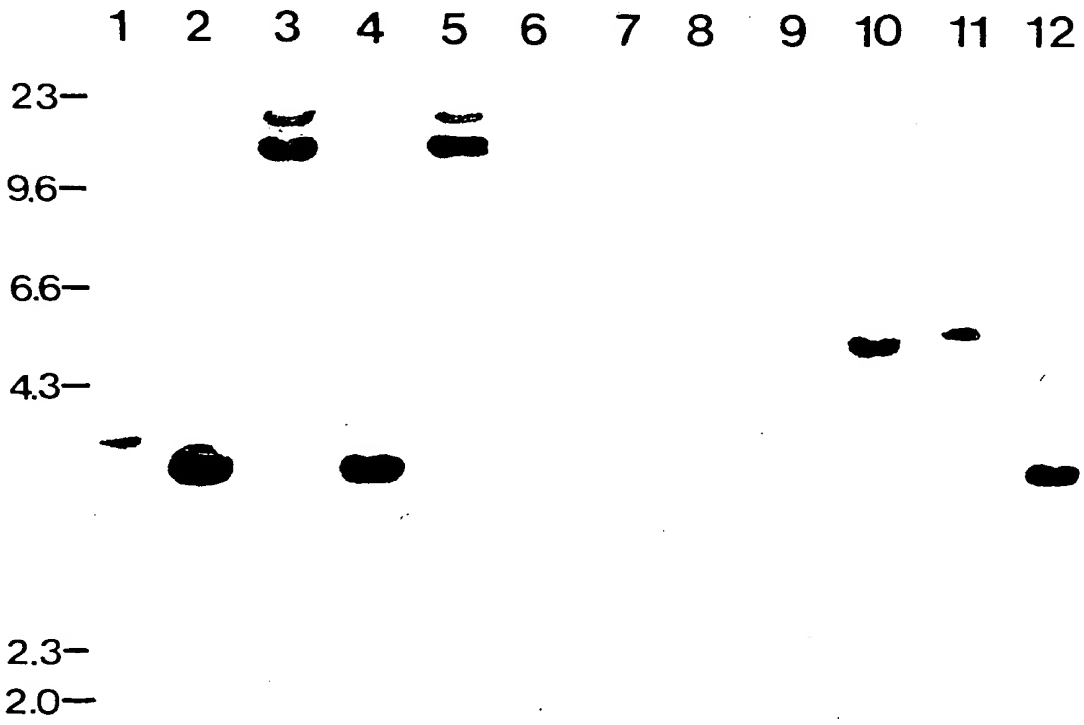
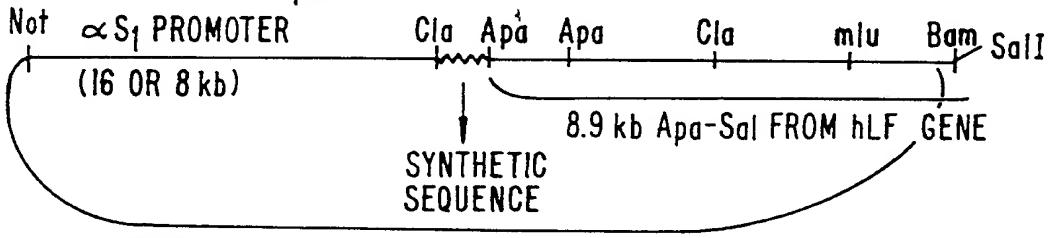


FIG. 12B.

O.G. FIG. | SUBCLASS | CLASS | APPROVED BY DRAFTSMAN

LIGATION PRODUCT OF p16kbCS AND SYNTHETIC SEQ. (Cla-Apa)+ hLF FRAGMENT (p8kbCS)



CLONING VECTOR: pkUN (4 kb)

CONSTRUCT NAME: 8 hLF gen 9k, OR 16 hLF gen 9k

FIG. 15A.

STRUCTURE OF ClaI-ApaI SYNTHETIC SEQUENCE

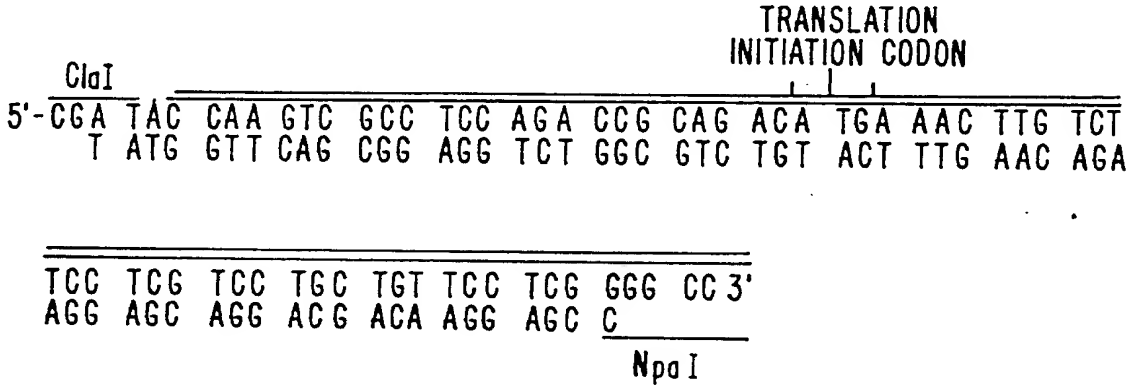
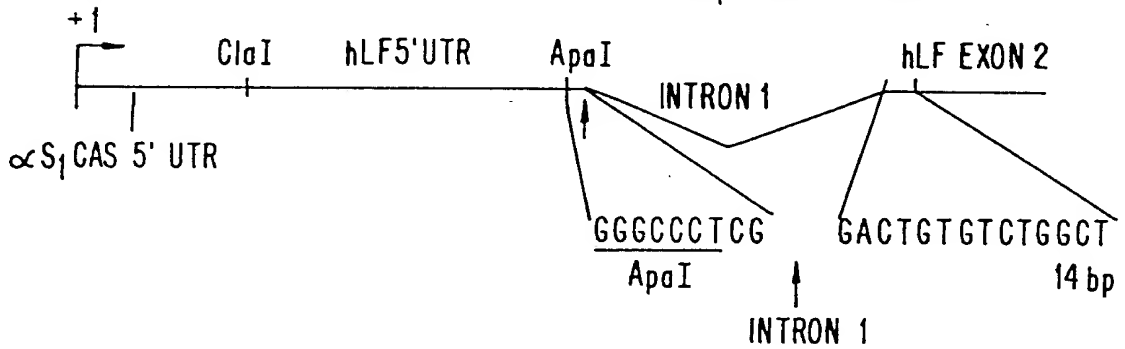


FIG. 15B.

+1: TRANSCRIPTION INITIATION SITE OF BOVINE αS_1 - CASEIN GENE



STRUCTURE OF REGION CONTAINING EXON 1 (HYBRID αS_1 - CASEIN/hLF EXON) AND PART OF EXON 2 OF THE GENOMIC hLF CONSTRUCTS DEPICTED IN FIGS. 15A THROUGH 17.

FIG. 15C.

O.G. FIG.
SUBCLASS
CLASS
APPROVED BY DRAFTSMAN

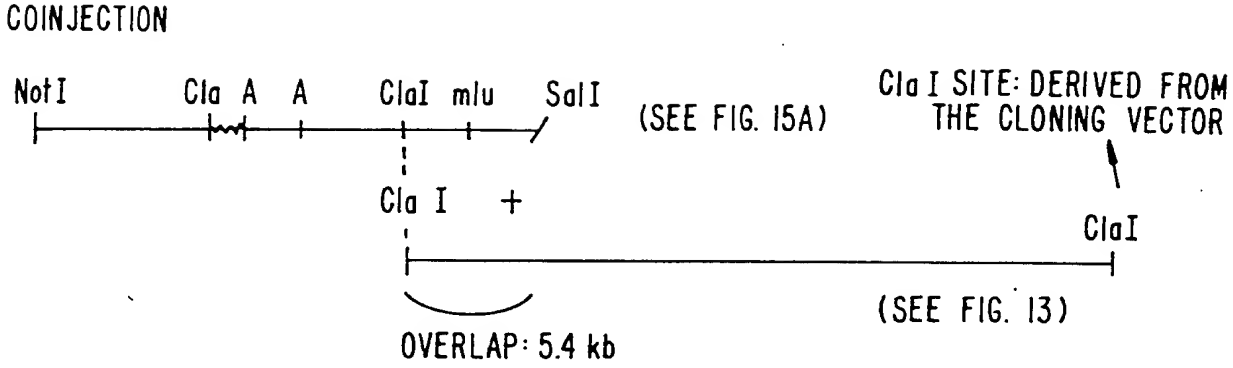
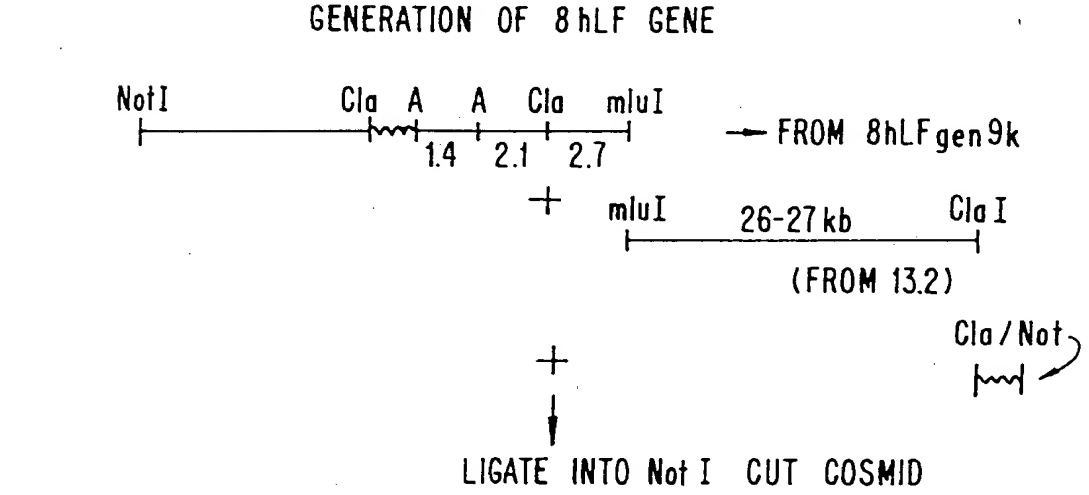


FIG. 16.



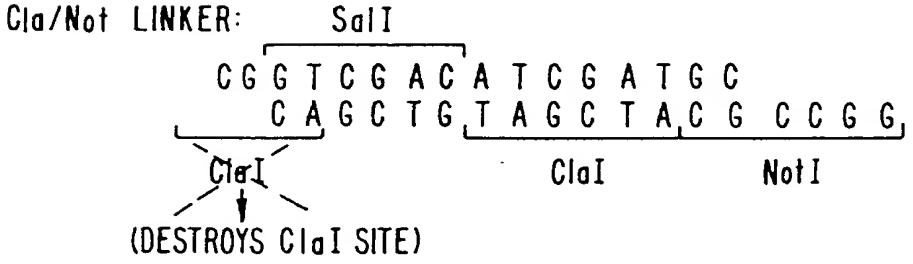


FIG. 17.

O.G. FIG. | CLASS | SUBCLASS
APPROVED BY DRAFTSMAN

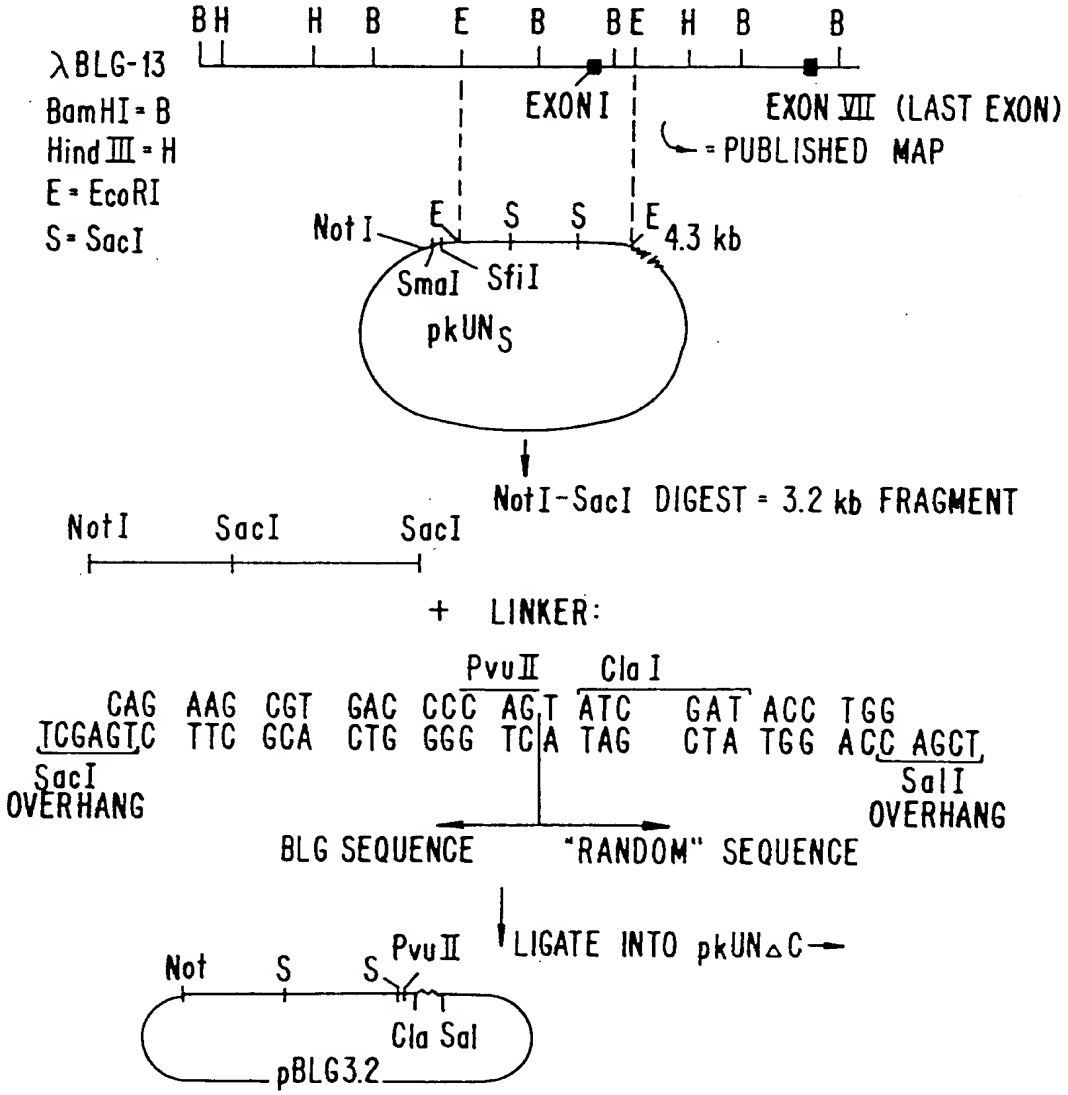


FIG. 18.

APPROVED BY DRAFTSMAN
O.G. FIG.
CLASS
SUBCLASS

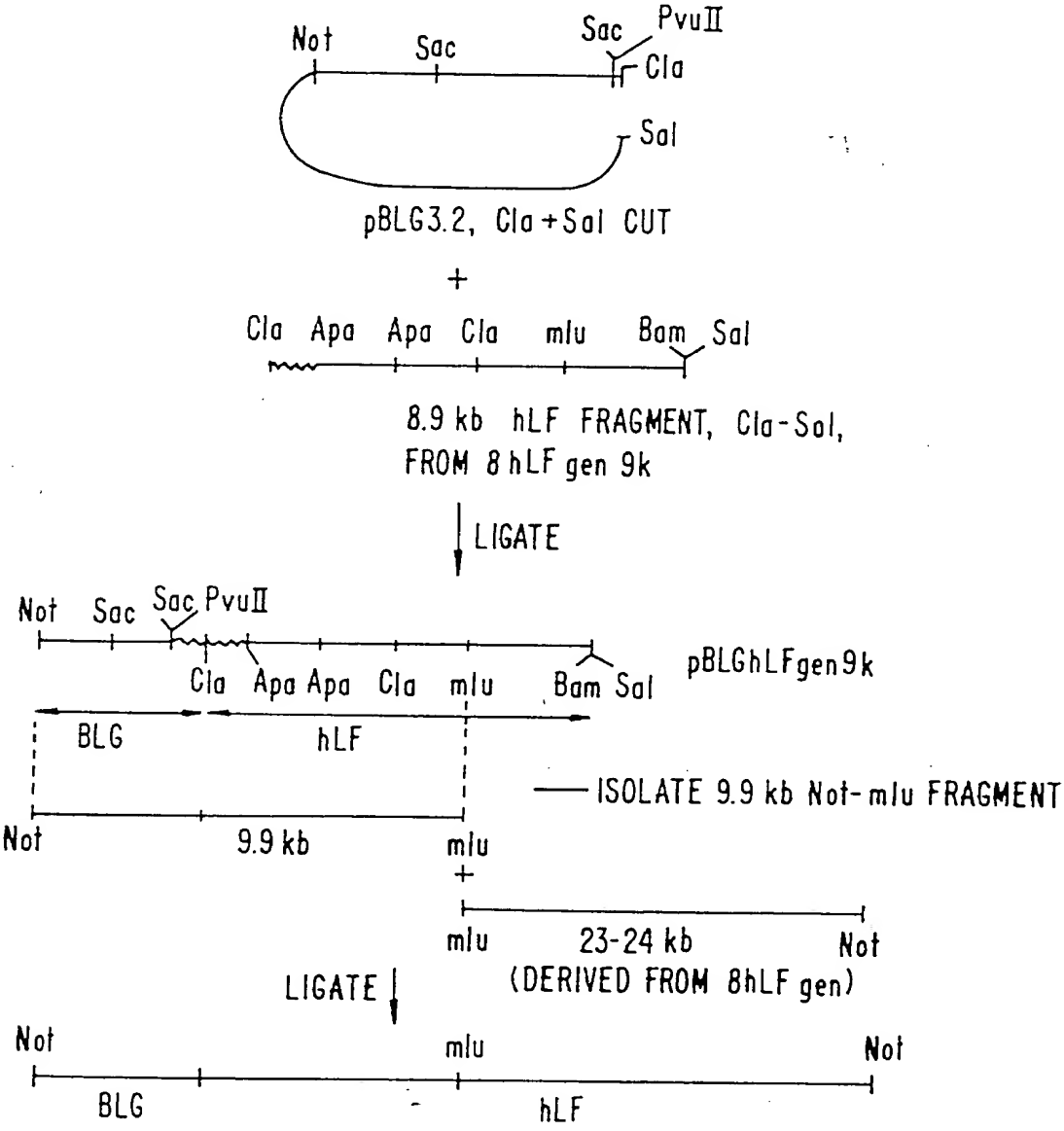


FIG. 19.

O.G. FIG.
CLASS SUBCLASS
APPROVED BY DRAFTSMAN

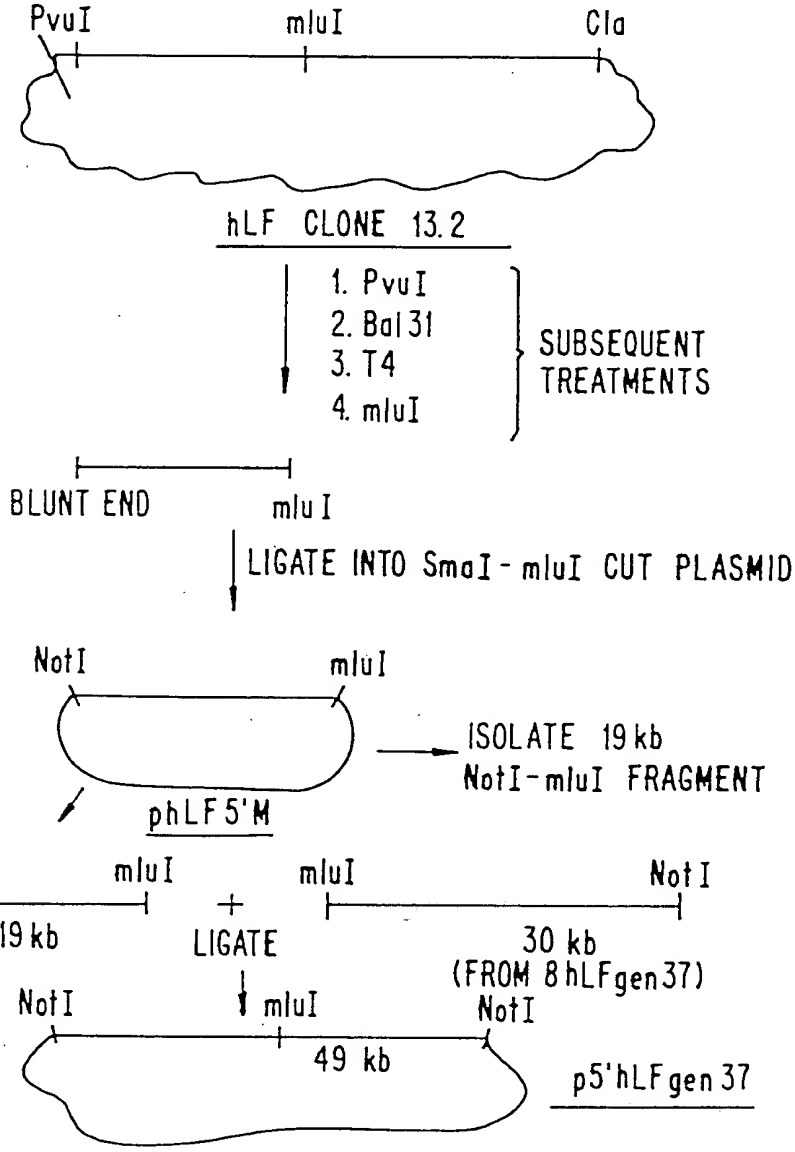
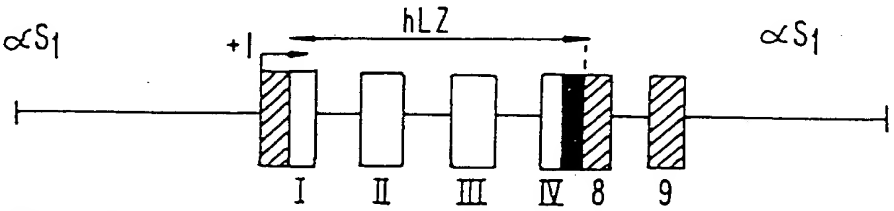


FIG. 20.

O.G. FIG.
CLASS
SUBCLASS
APPROVED
BY
DRAFTSMAN

DESIGN OF 16, 8 hLZ



▨ : EXON FROM αS_1 - CASEIN GENE (NON-CODING)

□ : EXON FROM hLZ GENE

+1: TRANSCRIPTION INITIATION SITE

■ : NON-CODING PART OF hLZ EXON 4

I, 8 AND 9: αS_1 - GENE EXON NUMBERS

I-IV : NUMBERS OF hLZ EXONS

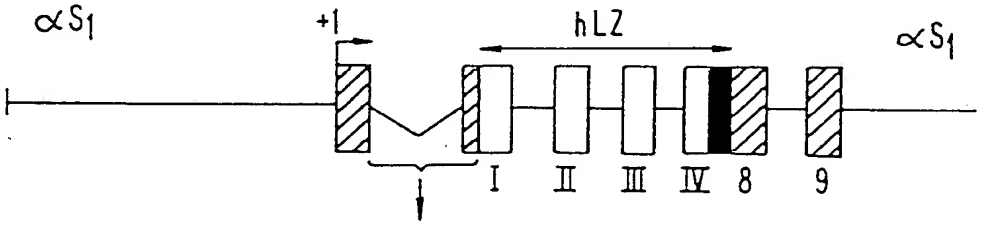
FLANKING REGIONS: FROM αS_1 CASEIN GENE

(SIGNAL SEQUENCE: hLZ)

FIG. 21.

DESIGN OF 16, 8 hLZ3

LEGEND: SEE FIGURE 9



HYBRID INTRON AND SPLICE ACCEPTOR SITE

(SIGNAL SEQUENCE: hLZ)

FIG. 22.

APPROVED BY DRAFTSMAN
O.G. FIG.
CLASS
SUBCLASS

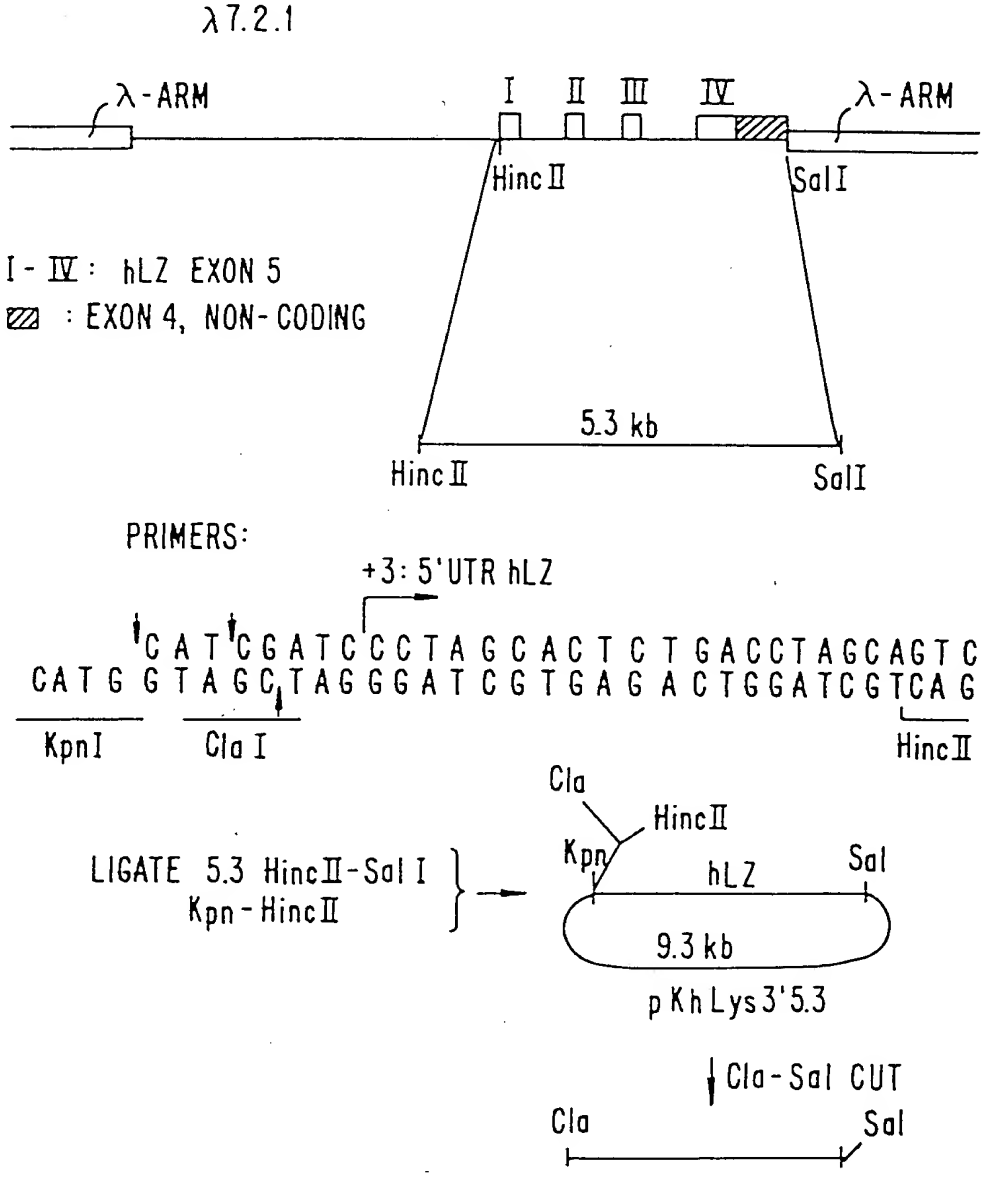


FIG. 23A.

O.G. FIG. | CLASS | SUBCLASS | APPROVED BY DRAFTSMAN

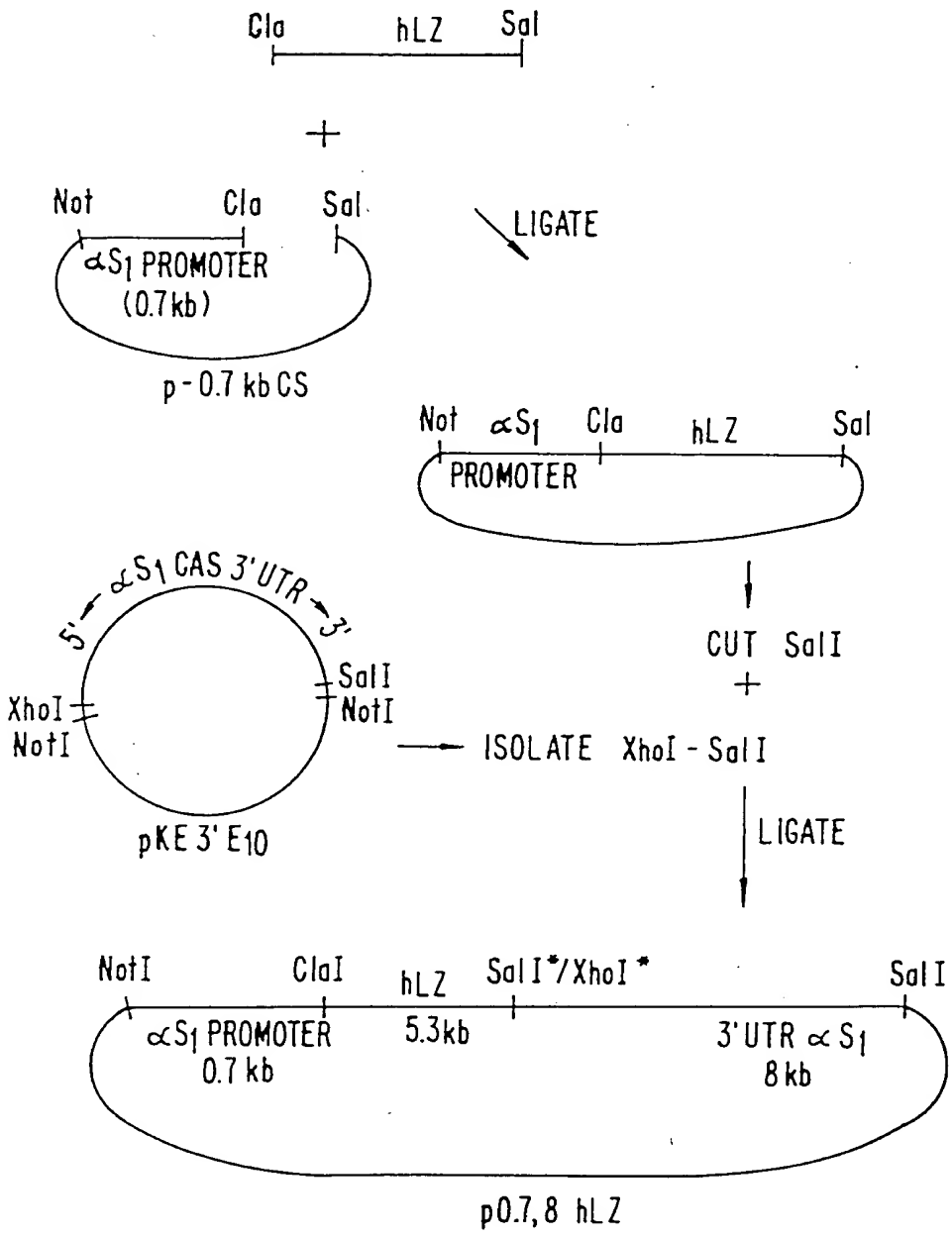


FIG. 23B.

APPROVED BY DRAFTSMAN | O.G. FIG. CLASS SUBCLASS

LINKER S_1/S_2:

SalI⊛ - NotI - SalI⊛

⊛: = DESTROYED SITE

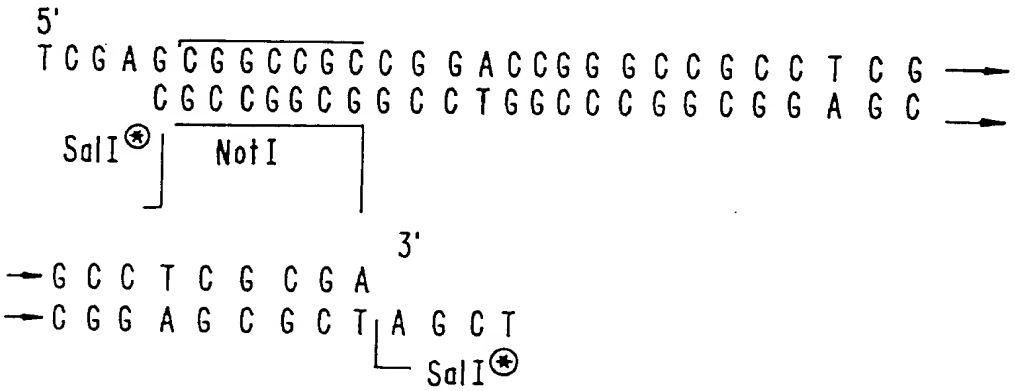


FIG. 23C.

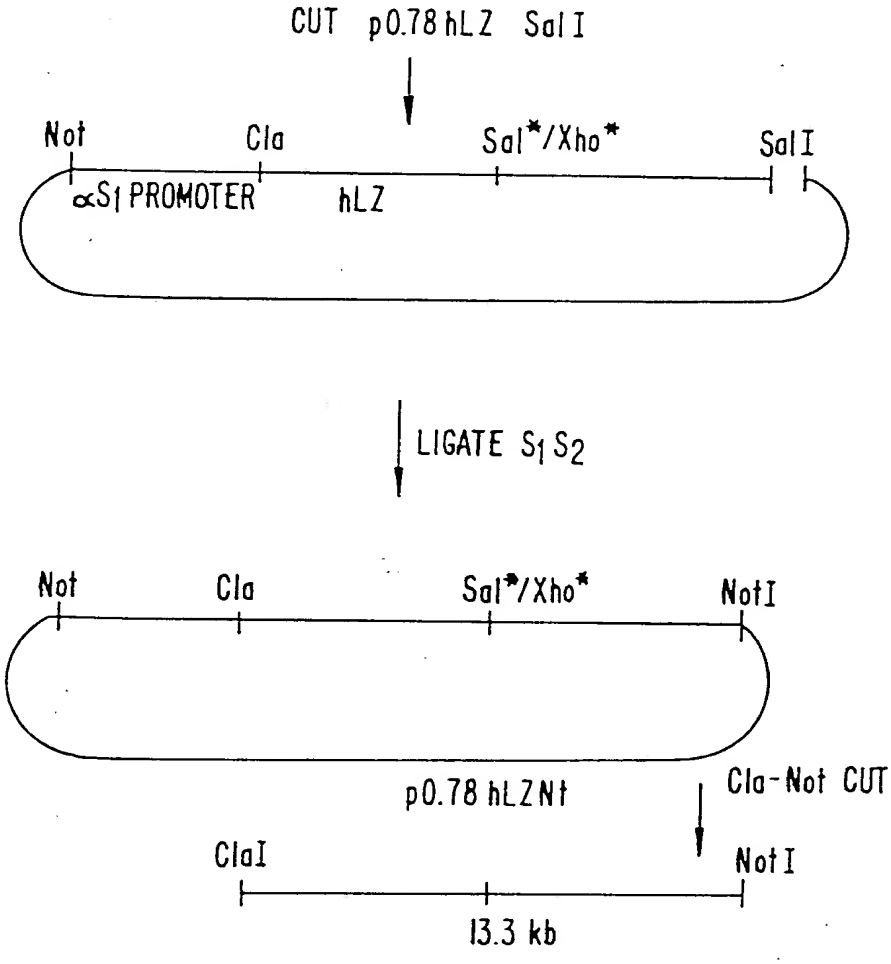


FIG. 23D.

APPROVED BY DRAFTSMAN
O.G. FIG.
CLASS
SUBCLASS

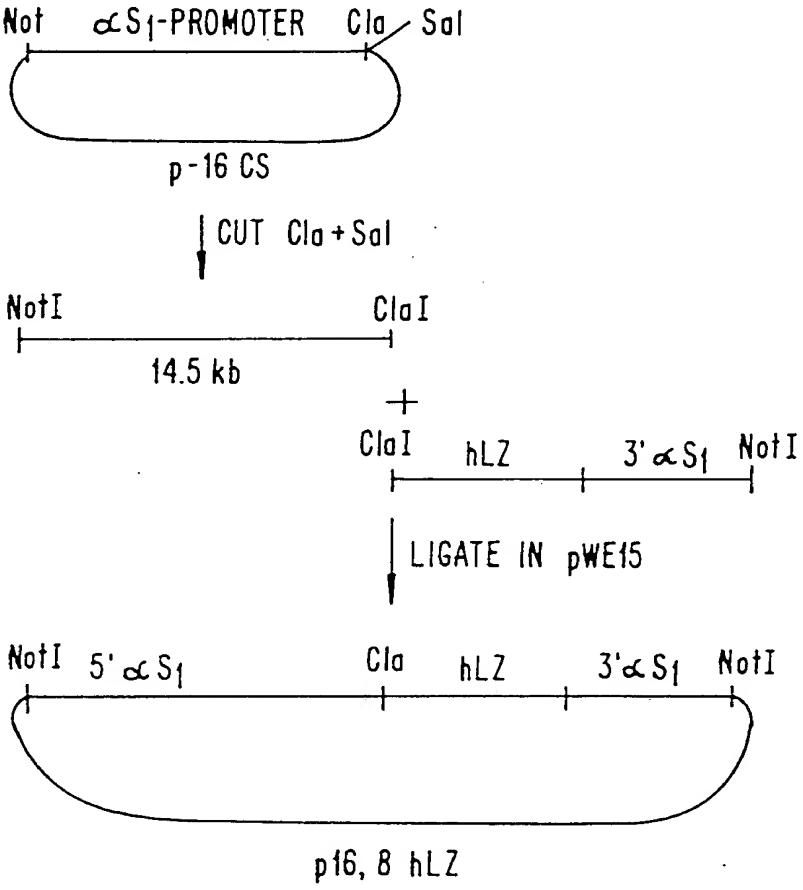


FIG. 23E.

APPROVED BY DRAFTSMAN
O.G. FIG.
CLASS
SUBCLASS

```
BOVINE 2 GGAAGTGCCTGGAGA...TTAAAATGTGAGAGTGGAGT....GGAGGTTG 44
         ||||||| |  | ||  ||||||||||||||||  | |     ||||||||
SHEEP 84 GGAAGTGTCCTGGGAGATTTAAAATGTGAGAGGCGGGAGGTGGGAGGTTG 133

      45 GGTCCTGTAGGCCTTCCCATCCCACGTGCCTCACGGAGCCCTAGTGCTAC 94
         || ||||| ||||| ||||||||||||||||      ||||| ||||||| |
     134 GGCCCTGTGGGCCTGCCCATCCCACGTGCCTGCATTAGCCCCAGTGCTGC 183

      95 TCAGTCATGCCCCCGCAGCAGGGGTCAGGTCACTTTCCCATCCTGGGGGT 144
         |||| | |||||||||| ||||||||||||||||||||| |||| |||||
     184 TCAGCCGTGCCCCCGCCGCAGGGGTCAGGTCACTTTCCCGTCCT.GGGGT 232

     145 TATTATGACTGTTGTCATTGTTGTTGCCATTTTTGCTACCCTAACTGGGC 194
         |||||||||| |||||||||   ||||||||||||||||||||||||||
     233 TATTATGACTCTTGTCATTGCCATTGCCATTTTTGCTACCCTAACTGGGC 282

     195 AGCGGGTGCTTGCAGAGCCCTCGATACTGACCAGGTTCCCCCCTCGGAGC 244
         ||| ||||||||||||||||||||||| ||||||| ||| ||||||||||
     283 AGCAGGTGCTTGCAGAGCCCTCGATACCGACCAGG.TCCTCCCTCGGAGC 331

     245 TCGACCTGAACCCCATGTCACCCTCGCCCCAGCCTGCAGAGGGTGGGTGA 294
         |||||||||||||||||||||||||| ||||||||||||||||||||||
     332 TCGACCTGAACCCCATGTCACCCTTGCCCCAGCCTGCAGAGGGTGGGTGA 381

     295 CTGCAGAGATCCCTTTACCCAAGGCCACAGTCACATGGTTTGGAGGAGAT 344
         |||||||||||||||| |||||||||||| |||||||||||||||||| |
     382 CTGCAGAGATCCCTTCACCCAAGGCCACGGTCACATGGTTTGGAGGAGCT 431

     345 GGTGCCCAAGGCAGAAGCCACCCTCCA.GACACACCTGCCCCCAGTGCTG 393
         |||||||||||||||| |||||||||| |||||||||| ||||||||||
     432 GGTGCCCAAGGCAGAGGCCACCCTCCAGGACACACCTGTCCCCAGTGCTG 481

     394 GCTCTGACCTGTCCTTGTCTAAGAGGCTGACCCCAGAAGTGTTCCTGGCG 443
         |||||||||||||||||||||||||||||||||||| ||||||||||||||
     482 GCTCTGACCTGTCCTTGTCTAAGAGGCTGACCCCGGAAGTGTTCCTGGCA 531

     444 CTGGCAGCCAGCCTGGACCCAGAGCCTGGACACCC.CCTGCGCCCCCACT 492
         |||||||||||||||||||||||| | ||||||| |||| |||||| ||
     532 CTGGCAGCCAGCCTGGACCCAGAGTCCAGACACCCACCTGTGCCCCCGCT 581

     493 TCTGGGGGCGTACCAGGAACCGTCCAGGCCCAGA..GGGCCTTCCTGCTT 540
         ||||||| | |||||||||||||| |||||||||  ||| ||||||||||
     582 TCTGGGGTC.TACCAGGAACCGTCTAGGCCCAGAGGGGGACTTCCTGCTT 630

     541 GGCCTCGAATGGAAGAAGGCCTCCTATTGTCCTTCGTAGAGGAAGCAACC 590
         ||||| | |||||||||||||||||||||||||| ||||||||||||| |||
     631 GGCCTTGGATGGAAGAAGGCCTCCTATTGTCC.TCGTAGAGGAAGCCACC 679

     591 CCAGGGCCCAAGGATAGGCCAGGGGGGGATTCGGGGAACCGCGTGGCT.CC 639
         || |||||  |||||  ||||  | |||||||  |||||||||||||| ||
     680 CCGGGGCCTGAGGATGAGCCAAGTGGGATTCCGGGAACCGCGTGGCTGGG 729

     640 GGCGCGGCCCGGGCTGGCTGGCTGGC..CCTCCTCCTGTATAAGGCCCCG 687
         ||| | |||||||||||||||||  ||   | ||||||||||||||||||
     730 GGCCCAGCCCGGGCTGGCTGGCCTGCATGCGCCTCCTGTATAAGGCCCCA 779
```

FIG. 24A.

APPROVED BY DRAFTSMAN | O.G. FIG. CLASS SUBCLASS

```
688  AGCCCG.CTGTCTCAGCCCTCCACTCCCTGCAGAGCTCAGAAGCGTGACC  736
     ||||| | ||||||||||||||||||||||||||||||||||||||||  ||||
780  AGCCTGCCTGTCTCAGCCCTCCACTCCCTGCAGAGCTCAGAAGCACGACC  829

737  CCAGCTGCAGCCATGAAGTGCCTCCTGCTTGC.....CCTGGCCCTCAC  780
     ||||||||||||||||||||||||||||||||||||||||||||||||
830  CCAGCTGCAGCCATGAAGTGCCTCCTGCTTGCCCTGGGCCTGGCCCTCGC  879

781  CTGTGGCGCCCAGGCCCTCATCGTCACC  808
     |||||||| ||||||| ||||||||||
880  CTGTGGCGTCCAGGCCATCATCGTCACC  907
```

*TRANSLATION INITIATION CODON

FIG. 24B.

LINKER GP 278/279

TRANSLATION START SITE (αS_1 SIGNAL SEQUENCE)

ClaI

CGATAACCATGAAACTTCTTATCCTCACCTGTCTTGTGGCTGTTGCTCTTG

TATT — ETC.

αS_1 — hLZ SEQUENCE

BalI

—CCAAGGTCTTTGAAAGGTGTGAGTTGC

ETC.—AACC

FIG. 25.

O.G. FIG. | CLASS | SUBCLASS
APPROVED BY DRAFTSMAN

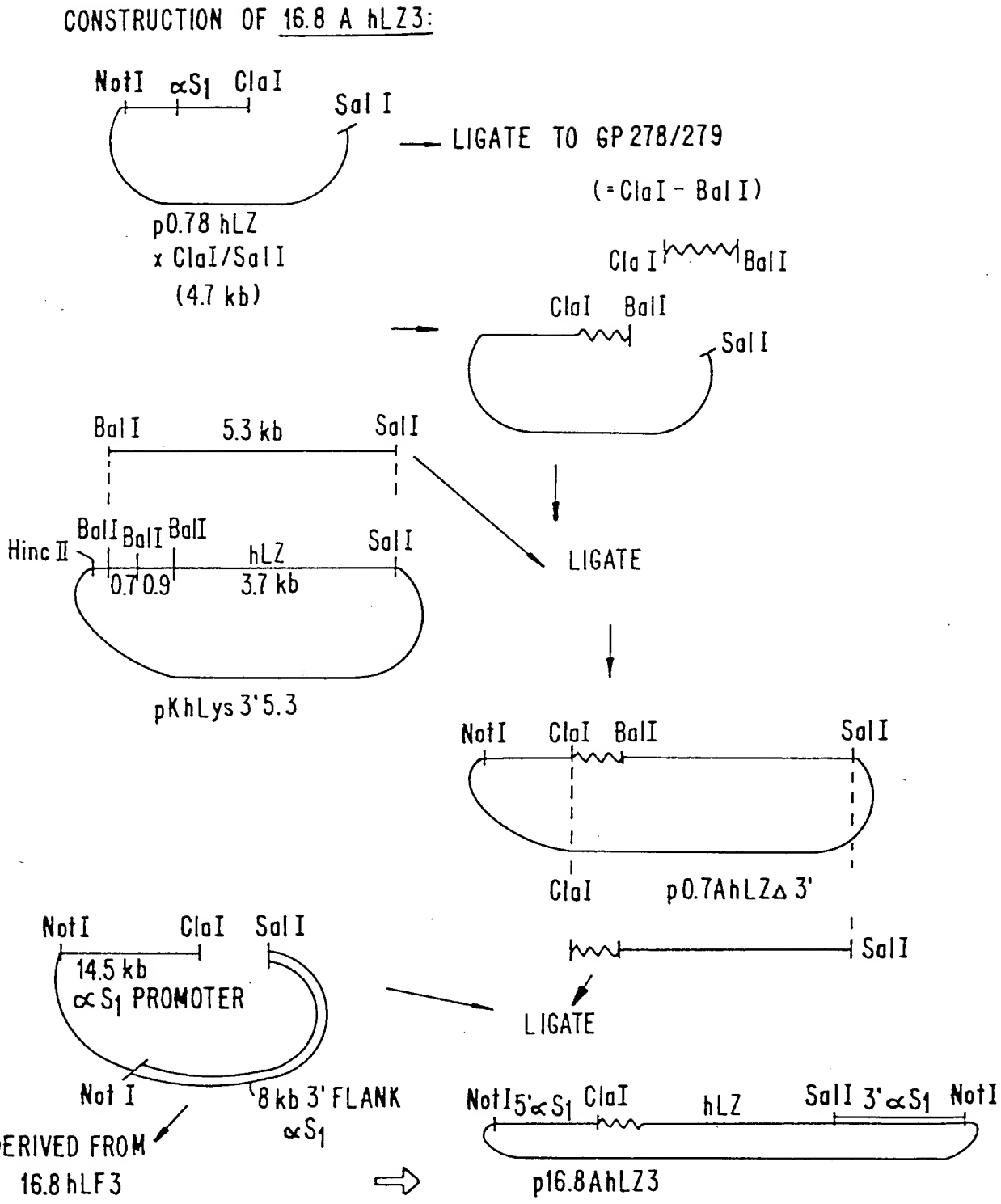


FIG. 26.

APPROVED BY DRAFTSMAN
O.G. FIG. CLASS SUBCLASS

CONSTRUCTION OF 16 A hLZ3:

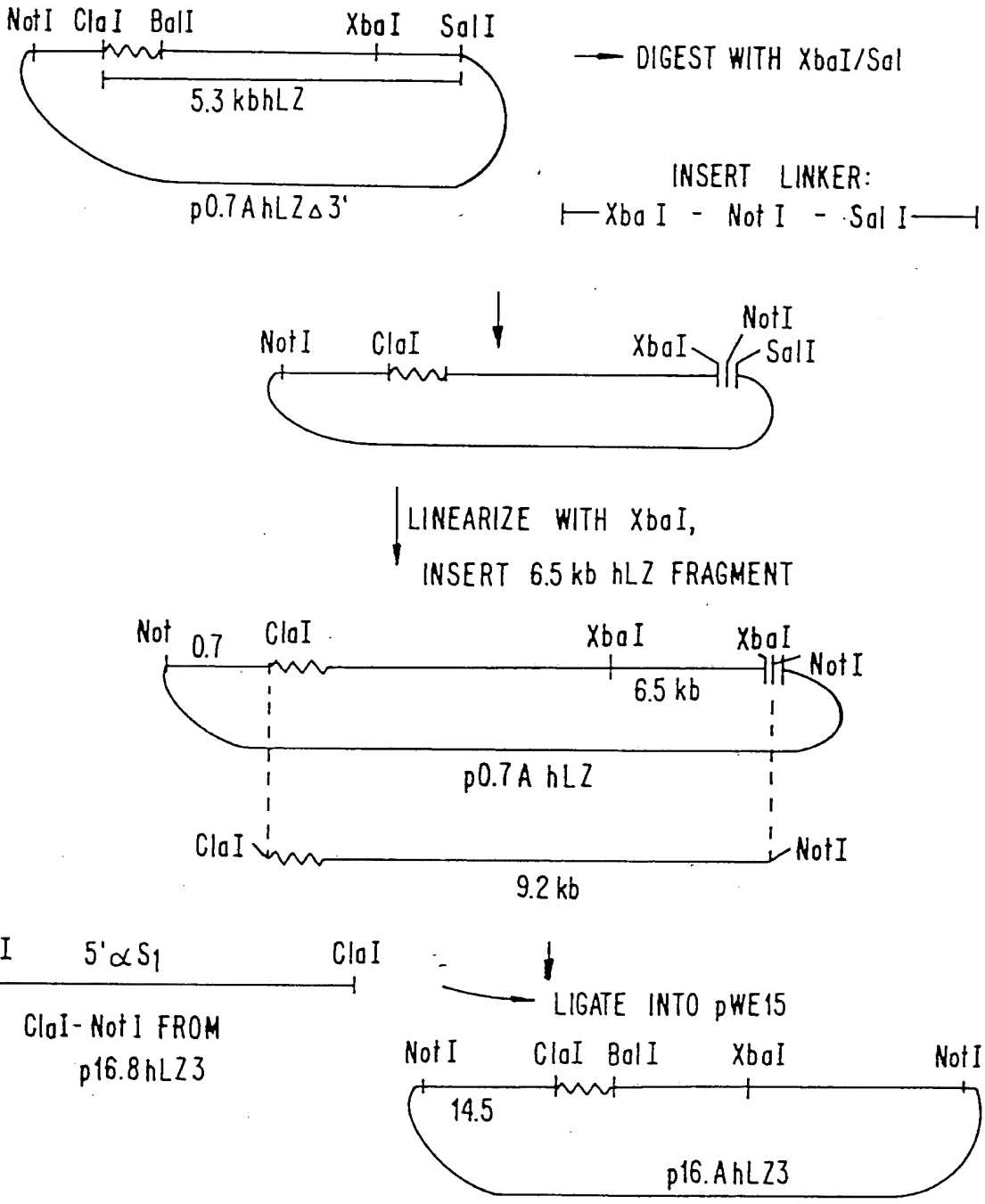


FIG. 27.